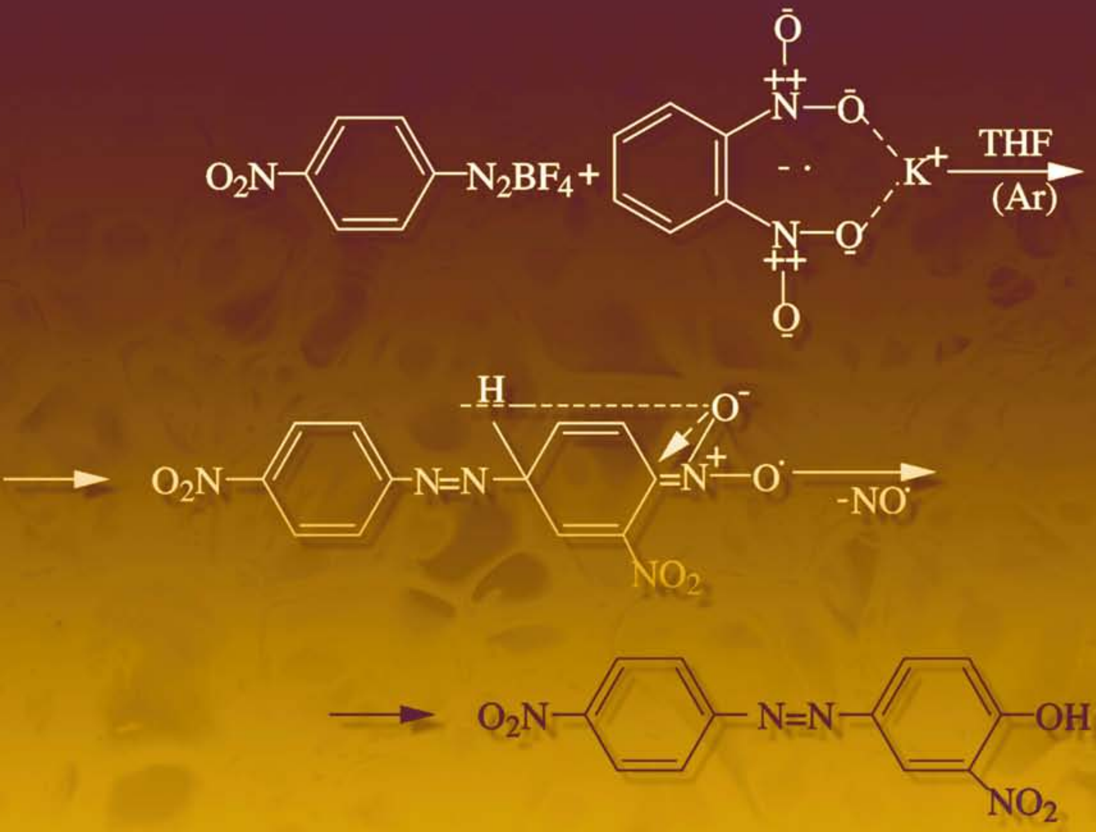
Ion-Radical Organic Chemistry

Principles and Applications

Second Edition



Zory Vlad Todres

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Dedication

To my wife Irina: the cloudless beauty of her heart, profundity of her mind, and depth of her feelings in all times have always provided reliable support to me.

For my children, Vladimir and Ellen, their mother represents a superior, stimulating example.

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Preface

Contemporary organic chemistry lays great emphasis on investigations of the structure and reactivity of intermediate species, originating in the reaction pathway from the starting compounds to the end products. Knowledge of the properties of the intermediary species and insight into the mechanism of reactions open new ways to increase the rates of formation and yields of the desired final products. Until recently, chemists focused their attention on neutral radicals or charged species of the ionic type. Particles having a combined nature of ions and radicals—ion-radicals—were beyond the scope of their investigations. Improved instrumental techniques markedly led to finer experiments. As a result, the species, which were little (if at all) known to the chemists of earlier decades, are now in the forefront.

Currently, the behavior of organic ion-radicals has become an area of interest. Ion-radicals are formed by one-electron oxidation or one-electron reduction of organic compounds in isolated redox processes and as intermediates along the pathways reactions. The conversion of an organic molecule into an ion-radical brings about a significant change in its electronic structure and corresponding alteration in its reactivity. This conversion allows the formation of necessary products under mild conditions with high yields at improved selectivity of transformation. In addition, there are several reactions that can proceed only through the ion-radical pathway and lead to products otherwise unobtainable.

The theme of this book is the formation, transformation, and application of ion-radicals in typical conditions of organic synthesis. Avoiding complex mathematics, this book presents an overview of organic ion-radical reactions and explains the principles of the ion-radical organic chemistry. Methods of determining ion-radical mechanisms and controlling ion-radical reactions are also reviewed.

Wherever applicable, issues relating to ecology and biomedical problems are addressed. The inorganic participants of the ion-radical organic reactions are also considered. Chapter 7 gives representative examples of synthetic procedures and considers the fundamentals of related synthetic approaches.

This book also provides a review of the current practical applications as well as an outlook on those predicted to be important in the near future. The reader will learn of the progress that has been made in technical developments by utilizing the organic ion-radicals. Electronic and optoelectronic devices, organic magnets and conductors, lubricants, other materials, and reactions of industrial or biomedical importance are considered.

Developments in organic chemistry of ion-radicals have been rapid. Thus, new interpretations of scientific data appear frequently in the literature. I have attempted to juxtapose the ideas from various references that complement one another, although the connections between them may not be immediately obvious. (An author index is included to help the readers find such connections in this book.)

Science is a collective affair and its main task is to produce trustworthy and generalized knowledge. My due apologies are to those authors who contributed to the development of this vast field but, for various reasons, have not been cited in this book. The contributors who are cited certainly do not reflect my preferences; their publications have been selected as illustrative examples that will allow the reader to follow the evolution of the corresponding topics.

Every new branch of science passes through several stages of progress, including the latent phase, phase of an increased interest, and phase of blooming and incorporating into its mother science as an integral part. Organic ion-radical chemistry has apparently passed through its initial phases (that spawned decades of heated debates). In recent years, the heat has simmered down. It was a result of the development of this branch of science and technology.

Having become a regular division of scientific knowledge, organic ion-radical chemistry is now entering the stage where the ideas elaborated are being implemented into general operation. It is now necessary to generalize the obtained data and treat them comprehensively. Grafting the new branch to the organic chemistry tree is the aim of this book.

I have worked in the field of organic ion-radicals and their applications for several decades and have become more and more fascinated by the beauty of this area and diversity it presents. Understanding the role of ion-radicals is as difficult as it is interesting. I hope that this attempt to graft this branch to the organic chemistry tree will be useful for both advancing basic research and facilitating new practical applications.

During my entire working life, I, like other researchers, have felt the pressure of the scientific community's judgment. Criticism is crucial! The writing of this book was aided by discussions with my colleagues and friends. I am indebted to all of them for their corrections and polemics. At the same time, their support was a great encouragement. I thank the publishers for initiating to publish the second edition of this book under the title *Ion-Radical Organic Chemistry: Principles and Applications*. The 7-year period after the first edition was so fruitful in terms of publication and has brought so many important benefits that some cardinal renewal of the book's material becomes inevitable. This second edition has been well updated to include the new subject area as well as new developments in the materials covered previously. Appropriate references are provided throughout.

Naturally, the subject development brings about some complications of the topics under consideration. Being concise enough, nonmathematical and not overly technical, the new edition consolidates knowledge from a number of disciplines to present a modern overview on ion-radical organic chemistry. This book is addressed to researchers and technologists who are carrying out syntheses and studying principles, governing the choice of optimal organic reaction conditions. It will be useful for physical organic chemists, ecologists, biologists, and specialists in microelectronics, as well as for professors, researchers, and students. I mean postgraduates, not fainthearted undergraduates (especially those final-year students who are preparing to enter the contemporary job market!).

By and large, people who are engaged in active work on synthetic or mechanistic organic chemistry and its practical applications will hopefully find this treatise informative and, perhaps, somewhat exciting.

Zory V. Todres

Author

Zory Vlad Todres holds an MSc and a PhD in chemistry and technology as well as a doctor habilitas in physical organic chemistry. Formerly, his career was divided between research (as a leading scientist at the Russian Academy of Sciences, Moscow) and delivering of lecture courses (as a professor at higher educational institutions in Russia). Having gained job experience from research organizations and industrial companies in the United States, he, presently, enjoys working as a science analyst at the American Chemical Society. Dr. Todres has been a guest speaker at many international conferences and has worked as a visiting scientist and lecturer for universities in the United States and abroad. His publications consist of 6 single-authored books, approximately 300 original papers and reviews, as well as 10 patents (2 of them in the market). He was awarded with a membership to the World Academy of Letters (the Einsteinian Chair of Science) and is cited in the *who's who* list of the United States and United Kingdom (particularly, in *American Outstanding Professionals*).

His book *Ion-Radical Organic Chemistry: Principles and Applications* (2003), preceding the present issue, gained a good rating in scientific publications. Some quotations from the reviews on the book are as follows:

> The book fills an important gap because charged radicals have not had fair share of the press. In its broad scope, it leads you into unfamiliar territory, you find a lot to question, but that itself is stimulating, and you are carried along by its infectious enthusiasm. The book opens up aspects of which you are ignorant, it is a good guide to relevant literature, and above all, the enthusiasm of the author carries through into the text (Alwyn Davies, *Alchemist*, Oct. 2003).

> The book's illustrations are mainly chemical formulae and reaction schemes, which are reader-friendly in respect of size and clarity (Laszlo Simandi, *React. Kinet. Catal Lett.* 79 (1), 209, 2003).

> The book should be available to students, particularly in a classroom setting, or simply as a resource book to have on their bookshelf. I recommend to purchase the book by libraries, at least (R. Daniel Little, *J. Am. Chem. Soc.* 125 (20), 6338, 2003).

> This is a book which, in my opinion, should find a place in the libraries of all universities and research institutes, where people are engaged in active research in synthetic or mechanistic organic chemistry. The task taken by the author was Herculean which the author has carried out with commendable skill, when he could bring in a reasonable amount of space, all the different aspects of ion-radical chemistry. The book is characterized by the lucidity of presentation, which has made it immensely readable (Asish De, *Indian J. Phys.* 77A (4), 401, 2003).

1 Nature of Organic Ion-Radicals and Their Ground-State Electronic Structure

1.1 INTRODUCTION

Organic chemistry represents an extensive volume of facts from which the contemporary doctrine of reactivity is built. The most important basis of this doctrine is the idea of intermediate species that arise along the way from the starting material to the final product. Depending on the nature of chemical transformation, cations, anions, and radicals are created midway. These species are formed mainly as a result of bond rupture. Bond rupture may proceed heterolytically or homolytically: $R–X \rightarrow R^- + X^+$, $R–X \rightarrow R^+ + X^-$, or $R–X \rightarrow R^\bullet + X^\bullet$.

Ions or radicals formed from a substrate further react with other ions or radicals. There are many reactions that include one-electron transfer before the formation of ions or radicals. Sometimes, electron transfer and bond cleavage can take place in a concerted manner. The initial results of one-electron transfer involve the formation of ion-radicals.

This book focuses on species of the type $(RX)^{\pm\bullet}$, that is, on cation- and anion-radicals. These terms were first introduced by Weitz (1928) ("Kationradikale" and "Anionradikale"). Currently, organic chemists differentiate that the anion-radicals originate from π and σ acceptors and the cation-radicals originate from π, σ, or n donors. These species are formed during reactions, when an organic molecule either loses one electron from the action of an electron acceptor or acquires one from the action of an electron donor: $R–X - e \rightarrow (R–X)^{+\bullet}$ or $R–X + e \rightarrow (R–X)^{-\bullet}$.

Ion-radicals differ from starting molecules only in the change of the total number of electrons; no bond rupture or bond formation occurs. From the following chapters, it is seen that after ion-radical formation, cleavage and association reactions often occur. Geometry changes on electron loss or gain can also take place. Reactions with the participation of ion-radicals bring their own, specific opportunities.

The concept of molecular orbitals (MOs) helps to explain the electron structure of ion-radicals. When one electron abandons the highest occupied molecular orbital (HOMO), a cation radical is formed. HOMO is a bonding orbital. If one electron is introduced externally, it takes the lowest unoccupied molecular orbital (LUMO), and the molecule becomes an anion-radical. LUMO is an antibonding orbital. Depending on the HOMO or LUMO involved in the redox reaction, organic donors appear as π, σ, or n species, whereas organic acceptors can be π or σ species. Sometimes, a combination of these functions takes place.

Ion-radicals have a dual character. They contain an unpaired electron and are, therefore, close to radicals. At the same time, they bear a charge and are, naturally, close to ions. This is why the words "ion" and "radical" are connected by a hyphen. Being radicals, ion-radicals are ready to react with strange radicals. Like all other radicals, they can dismutate and recombine. Being ions, ion-radicals are able to react with particles of the opposite charge, and are prone to form ionic aggregates. In contrast to radicals, the ion-radicals are specially sensitive to medium effects.

Equal or nonuniform distribution of spin density can occur among individual atoms of the molecular carcass. This kind of distribution defines the activity of one or another position in an ion-radical. From the point of view of organic synthesis, properties of ion-radicals such as stability, resistance to active medium components, capacity to disintegrate in the required direction, and

the possibility of participating in electron exchange are especially important. All these properties become understandable (or predictable in cases of unknown examples) from the organic ion-radical electronic structure. Therefore, the discussion will be based on the analysis of connections between the structure of ion-radicals and their reactivity or physical properties. This chapter concerns the peculiarities of conjugation, electronic structures, and acid–base properties of ion-radicals originated from molecules of various chemical classes.

1.2 UNUSUAL FEATURES

1.2.1 Substituent Effects

This section shows that substituent effects in organic ion-radicals are quite different from those of their parent neutral molecules. Amino and nitro compounds are good examples to show that conventional ideas may not be applicable to the chemistry of ion-radicals.

N,*N*-dimethylaniline is a molecule with a lone electron pair on the nitrogen atom. Of course, there is a strong interaction between this pair and the π electron system of the benzene ring. We often place the symbol of the cation-radical ($^{+\bullet}$) on the nitrogen atom. However, according to the *ab initio* Hartree–Fock molecular orbital calculations (Zhang et al. 2000), this nitrogen atom is in fact negatively charged (−0.708) and the positive charge is distributed on the carbon atoms, especially on the two methyl groups (+0.482 on each). Influenced by the positive-charge delocalization along the cation-radical, the benzene ring becomes an electron-deficient unit with a positive charge of +0.744. Summation yields the total charge of +1 for the *N*,*N*-dimethylaniline cation-radical.

Naturally, the cation-radical of diphenylamine is characterized with an analogous positive-charge delocalization (Liu and Lund 2005). The *N*,*N*′-diphenyl-*p*-phenylenediamine cation-radical is almost planar and the spin density intrudes outer phenyls. When the outer phenyls contain two methyl groups in ortho positions, the molecule loses planarity. As a result, the spin density concentrates within the inner ring and its adjacent two nitrogen atoms (Nishiumi et al. 2004).

In the trication-triradical of 1,3,5-triaminobenzene, quantum-chemical calculations indicate that the positive charges are very much delocalized into the benzene core, whereas the nitrogen atoms bear negative charges (Nguyen et al. 2005).

In the anion-radicals of nitro compounds, an unpaired electron is localized on the nitro group and this localization depends on the nature of the core molecule bearing this nitro substituent. The value of the hyperfine coupling (HFC) constant in the electron-spin resonance (ESR) spectrum reflects the extent of localization of the unpaired electron; a^N values of several nitro compounds are given in Table 1.1.

Let us compare HFC data from Table 1.1. Aliphatic nitro compounds produce anion-radicals, in which an unpaired electron spends its time on the nitro group completely. In the nitrobenzene

TABLE 1.1
Nitrogen HFC Constants (a^N) from Experimental ESR Spectra of Nitro Compounds

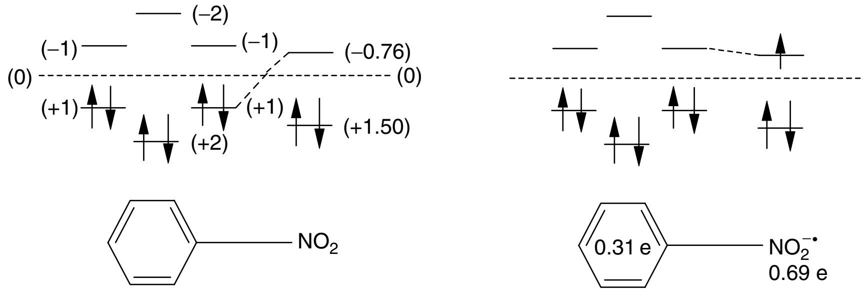
Compounds	Constant a^N (mT)	References
Nitroalkanes	2.4–2.5	Stone and Maki (1962), McKinney and Geske (1967)
Nitrobenzene	1.0	Geske and Maki (1960)
2-Chloronitrobenzene	0.9	Starichenko et al. (2000)
2,6-Dichloronitrobenzene	1.4	Starichenko (2000)
Nitrodurene	2.0	Geske and Ragle (1961)

anion-radical, an unpaired electron is partially delocalized on the aromatic ring due to conjugation. As observed, the HFC constant decreases by a half as compared to the aliphatic counterparts. Diminution of the π conjugation in the $PhNO_2$ system as a result of the nitro group distortion leads to the localization of the unpaired electron on the nitro group. In the nitrobenzene anion-radical, however, an unpaired electron is not evenly spread between the nitro group and the benzene ring. This anion-radical has most of the spin density (65–70%) localized on the nitro group (Stone and Maki 1962, Kolker and Waters 1964). These values are based on the values of a^N and a^H constants from the ESR spectrum of the nitrobenzene anion-radical. Molecular orbital calculations within the Hueckel approximation predict the same spin distribution: 0.31 of the unit-spin density over the phenyl nucleus and 0.69 on the nitro group (Todres 1981). The recent calculation of the nitrobenzene anion-radical shows that, in terms of Hirshfeld charges, the nitro group bears 0.782 and the phenyl group dissipates 0.218 parts of the unit negative charge (Baik et al. 2002).

Of course, it is the entire molecule that receives an electron on reduction. However, the nitro group is the part where the excess electrons spend the majority of their time. Consideration of quantum-chemical features of the nitrobenzene anion-radical is of particular interest. The model for the calculation includes a combination of fragment orbitals for Ph and NO_2, and the results are represented in Scheme 1.1. The left part of the scheme refers to the neutral $PhNO_2$ and the right part refers to the anion-radical, $PhNO_2^{-\bullet}$ (Todres 1981).

Some changes in the total orbital energy take place on the one-electron placement on the LUMO. According to the calculations, relative energy gaps remain unchanged for the orbitals in the nitrobenzene anion-radical, if compared with those of the parent nitrobenzene. For the sake of graphic clarity, Scheme 1.1 disregards the difference mentioned, keeping the main feature of equality in the energy gaps.

The nitro group in the parent nitrobenzene evidently acts as the π acceptor, which pulls the electron density out of the aromatic ring. An unpaired electron will obviously occupy the first vacant π orbital of the nitro fragment (i.e., the lowest-energy-fragment orbital). Interaction between the occupied orbital and the vacant one (the absolutely empty orbital) is the most favorable. In the nitrobenzene anion-radical, the one-electron-populated fragment orbital of $NO_2^{-\bullet}$ will send the spin density to the ring. Such an interaction is very advantageous because the lowest vacant ring orbital and the highest occupied orbital of $NO_2^{-\bullet}$ are close with respect to their energy levels. Therefore, the nitro group can, in fact, act as a π donor in the nitrobenzene anion-radical. This prediction is not self-evident since the nitro group in neutral aromatic nitro compounds is recognized as a strong π acceptor and, in principle, even as a reservoir of four to six additional electrons. Comparing the half-wave potentials of reversible one-electron reduction of *m*-dinitrobenzene and other meta-substituted nitrobenzenes, one can determine the Hammett constant for the $NO_2^{-\bullet}$ group. When the NO_2 group is transformed into the $NO_2^{-\bullet}$ group, a change in both the sign and value of the correlation constant is observed (Todres et al. 1972a, 1972b). Formal comparison of the Hammett constants for NO_2, $NO_2^{-\bullet}$, and NH_2 groups shows that $NO_2^{-\bullet}$ is close to NH_2 in terms of donating ability: $\sigma_m(NO_2) = +0.71$,



SCHEME 1.1

$\sigma_m(NO_2^{-\bullet}) = -0.17$, and $\sigma_m(NH_2) = -0.16$. It was checked that the obtained value of $\sigma_m(NO_2^{-\bullet})$ is statistically reliable.

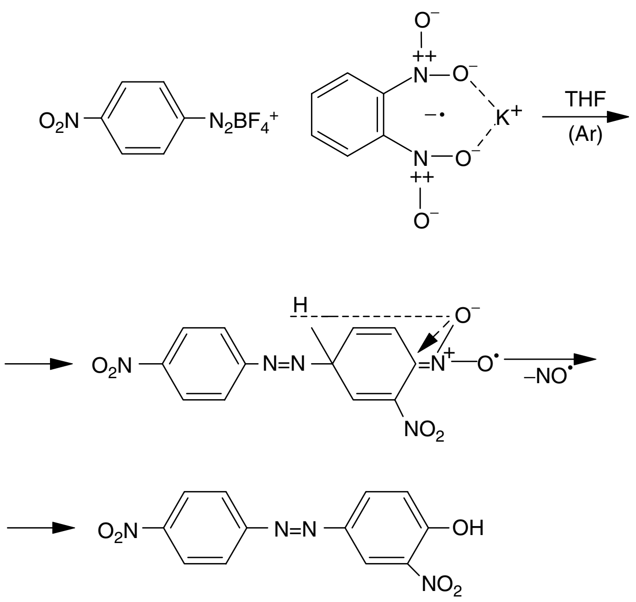
Leventis et al. (2002) studied the electrochemical reduction of 4-(4-substituted-benzoyl)-*N*-methylpyridinium cations. The authors demonstrated two chemically reversible, well-separated one-electron waves for all except the 4-(4-nitrobenzoyl)-*N*-methylpyridinium cation. The latter underwent not two, but three one-electron reductions and the first wave corresponded to NO_2 transformation into $NO_2^{-\bullet}$. Correlating the third-wave potential of the nitro representative to the second-wave potentials of the others, Leventis et al. determined $\sigma_p(NO_2^{-\bullet})$. The statistically weighed value of $\sigma_p(NO_2^{-\bullet})$ was found to be -0.97. For comparison, $\sigma_p(S^{-\bullet})$ is equal to -1.21. It is worth noting that $\sigma_m(NO_2^{-\bullet}) = -0.17$ and $\sigma_p(NO_2^{-\bullet}) = -0.97$ were established in the framework of the same experimental approach although with a time lag of 30 years.

Considering the gas-phase electronic structure of the *m*-dinitrobenzene anion-radical, all the scientists since 1960 assumed that an unpaired electron is distributed between the two nitro groups equally. The recent calculations (by means of Hartree-Fock method) provide a strong asymmetrical picture: The reduced $CNO_2^{-\bullet}$ fragment has a charge of -0.66 and the other CNO_2 fragment has a charge of -0.35 (Nelsen et al. 2004). The charge of -0.66 on the reduced fragment of *m*-dinitrobenzene is close to the magnitude of $-(0.65-0.70)$ for the reduced $CNO_2^{-\bullet}$ fragment in mononitrobenzene mentioned earlier. A multiconfigurational quantum chemical study by Mikhailov et al. (2005) also shows that the more stable structure of the *m*-dinitrobenzene anion-radical has an asymmetrical geometry and an unpaired electron is localized on one nitro group. Thus, various theoretical considerations completely coincide with the experiments and particularly with the result obtained from the Hammett correlation (Todres et al. 1972a, 1972b).

Having captured the single electron, the nitro group then acts as a negatively charged substituent. Similarly, the stable anion-radical resulting from aryl diazocyanides $[(ArN{=}NCN)^{-\bullet}]$ contains a substituent $[(N{=}NCN)^{-\bullet}]$ that interacts with the aryl ring as a donor (Kachkurova et al. 1987). Using other nitro derivatives of an aromatic heterocyclic series, the generalization and statistical relevance of the observed $\sigma_m(NO_2^{-\bullet})$ constant were established (Todres et al. 1968, Todres et al. 1972a). The sign and absolute magnitude of the Hammett constant are invariant regardless of which cation (K^+, Na^+, or Alk_4N^+) in the anion-radical salts of nitro compounds was studied. Such invariance is caused by the linear dependence between electrochemical reduction potentials of substituted nitrobenzenes and the contribution of the lowest vacant π^* orbital of the nitro group to the π orbital of this anion-radical, which is occupied by the single electron (Koptyug et al. 1988).

In the sense of chemical reactivity, the ability of nitrobenzene anion-radicals undergoing coupling with benzene diazo cations has been studied (Todres et al. 1988). This reaction is known to proceed for aromatic compounds having donor-type substituents (NH_2, OH). Aromatic compounds containing only the nitro group do not participate in azo-coupling. It is also worth noting that benzenediazo cations are strong electron acceptors. For instance, the interaction between benzene or substituted benzene-diazonium fluoroborates and the sodium salt of the naphthalene anion-radical results in electron transfer only (Singh et al. 1977). The products are naphthalene (from its anion-radical) and benzene or its derivatives (from benzene or substituted benzene-diazonium fluoroborates). Potassium nitrobenzene anion-radical also reacts with diazonium cations according to the electron-transfer scheme. Products of azo-coupling were not found (Todres et al. 1988).

To detain an unpaired electron and facilitate the azocoupling, the *o*-dinitrobenzene anion-radical was tested in the reaction (Todres et al. 1988). Such an anion-radical yielded an azo-coupled product according to Scheme 1.2 (the nitrogen oxide evolved was detected). The reaction led to a para-substituted product, entirely in accordance with the calculated distribution of spin density in the anion-radical of *o*-dinitrobenzene (Todres 1990). It was established, by means of labeled-atom experiments and analysis of the gas produced, that azo-coupling is accompanied by the conversion of one of the nitro groups into the hydroxy group and the liberation of nitric monoxide. In other

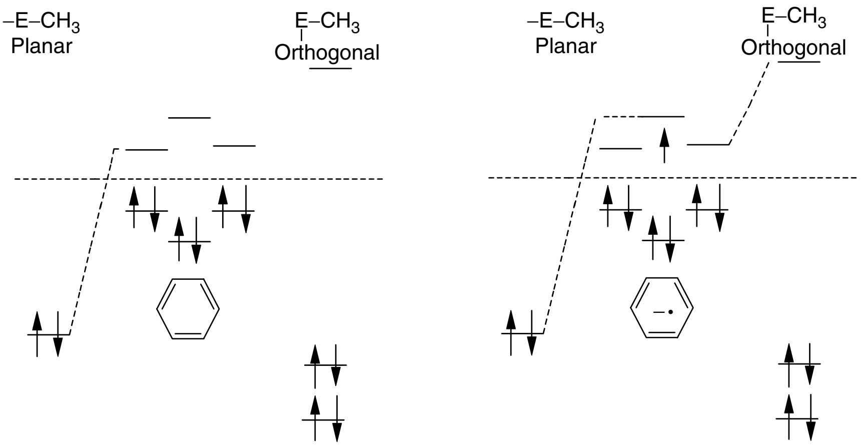


SCHEME 1.2

words, the initial radical product of azo-coupling is stabilized by elimination of the small nitrogen monoxide radical to give the stable nonradical final product (Todres et al. 1988; Scheme 1.2).

Transformation of the parent molecule to the corresponding anion-radical changes substituent effects not only for the nitro group but also for other substituents. We have just observed the opportunity of using the nitro group as a donor (not as an acceptor) in the anion-radicals of aromatic nitro compounds. In the case of AlkO and AlkS substituents, we have a chance of encountering the donor-to-acceptor transformation of the thioalkyl group after one-electron capture by thioalkylbenzenes (Bernardi et al. 1979). Both the groups, AlkO and AlkS, are commonly known as electron donors. However, in the anion-radical form, these groups exert nonidentical effects. The methoxy group maintains its donor properties, whereas the methylthio group exhibits acceptor properties. This is evident from the comparison of the ESR spectra of the nitrobenzene anion-radical with its derivatives, in particular the MeO- and MeS-substituted ones. The introduction of substituents into nitrobenzene, in general, affects the value of a^N arising from the splitting of an unpaired electron by the nitrogen atom in the anion-radical (see, e.g., Kukovitskii et al. 1983, Pedulli and Todres 1992, Yanilkin et al. 2002, Ciminale 2004). If the group introduced is a donor, the $a^N(NO_2)$ value increases. If it is an acceptor, then the $a^N(NO_2)$ value decreases. As follows from such a comparison of a^N constants, the MeO and EtO groups act similar to the Me or S^- groups (donors). At the same time, the MeS and EtS groups act similar to CN, SO_2Me, and SO_2Et groups (acceptors) (Ioffe et al. 1970, Alberti et al. 1977, 1979, Bernardi et al. 1979).

The sharp contrast between the electronic effects exerted by the oxyalkyl and thioalkyl groups in aromatic anion-radicals was explained by means of group orbital-energy diagrams. The usual mechanism involving n, π conjugation requires the MeO or MeS group to be situated in the same plane as the aromatic ring of the parent (neutral) molecules. According to the calculations by Bernardi et al. (1979), "the most stable conformation is the planar" for the anion-radical of anisol. In the case of the anion-radical of thioanisol, however, "the preferred conformation is orthogonal." The planar conformation is stabilized by the usual n, π conjugation between the benzene ring and oxygen or sulfur. Such n, π conjugation is impossible in the orthogonal arrangement, and only the σ electrons of the sulfur or oxygen appear to be involved. Only the σ orbitals of these atoms are



SCHEME 1.3

symmetrically available for overlapping with the benzene π orbitals when fragments of the molecule are oriented perpendicularly. However, interaction between the π electrons of the benzene ring and the vacant σ* orbitals of the substituent is also possible in principle because this interaction is symmetrically allowed. In practice, σ, π and σ*, π interactions are not too important in the case of uncharged molecules, since the gap between the benzene π orbitals and σ/σ* orbitals of the substituents is too wide. This is obvious from the left part of Scheme 1.3.

Conversion of a neutral molecule into an anion-radical leads to occupation of the vacant orbital of the lowest energy. This orbital is the π orbital of the benzene ring in both anisole and thioanisole. Charge transfer is possible only by means of an interaction between the vacant and occupied orbitals and only if an energy gap between them is not too wide. As the σ* orbitals of the anisole MeO group are very far away from the π orbital occupied by the single electron, the conjugation conditions in the anion-radical compared to the neutral molecule remain unchanged. This is evident from the right part of Scheme 1.3.

In thioanisole, the MeS group differs from the MeO group of the anisole in the fact that the σ* orbital is posed at a lower energy level (Alberti et al. 1979). In this case, the population of the lowest vacant aromatic π orbital by a single electron changes the conjugation conditions. The σ*, π interaction becomes more favorable than the n, π interaction because the energy gap between the σ* and π orbitals is narrower. In other words, conditions created in the anion-radical promote charge transfer from the ring to the substituent rather than from the substituent to the ring, as in the case of the neutral molecule. This is why the orthogonal conformation is stabilized instead of the planar one. The conversion of thioanisole into the anion-radical causes the change in the orientation of the thiomethyl group relative to the aromatic ring plane. This is depicted on the right part of Scheme 1.3. Once again, not the energy level but the relative energy gaps remain unchanged for these anion-radicals as compared to the parent molecules.

In the case of thioanisole cation-radical, ESR spectroscopy (Alberti et al. 1984) and B3LYP calculations (Baciocchi and Gerini 2004) convincingly indicate that the planar conformation is by far the most stable. In the cation-radical, the thiomethyl group remains, in expectation, an electron-donating substituent.

For phenyl methyl sulfoxide (PhSOMe) and its cation-radical [$(PhSOMe)^{+\bullet}$], the parameters of molecular structure are close to one another (Baciocchi et al. 2006b). In PhSOMe, the HOMO resides on the SOMe group (Csonka et al. 1998). Approximately 70% of the charge and spin density are on S and O in $(PhSOMe)^{+\bullet}$; the positive charge is mainly localized on S, whereas the most significant fraction of the spin is on O (Baciocchi et al. 2006a). Typically, cation-radicals bearing the methyl group react with ^{-}OH as C–H acids giving $-CH_2OH$ derivatives. The cation-radical

$(PhSOMe)^{+\bullet}$, however, reacts with hydroxide in a different way, adding ^{-}OH to the S atom—just to the atom that bears the significant part of positive charge in this species (Baciocchi et al. 2006b).

Intriguing results were obtained for ion-radicals of allyltrimethylsilane (Egorochkin et al. 2007). In the neutral system of $H_2C{=}CHCH_2SiMe_3$, CH_2SiMe_3 substituent exhibits the resonance donor and acceptor properties toward the $H_2C{=}CH$ fragment simultaneously. The resonance donor effect of the σ, π conjugation, that is, of interaction between the σ orbital of CH_2–Si moiety and the π orbital of C=C bond, prevails. On going to the cation-radical $H_2C{=}CH^{+\bullet}{-}CH_2SiMe_3$, the σ, π conjugation is seriously enhanced. For CH_2SiMe_3, $\sigma_R = -0.24$ increases up to $\sigma_R = -0.65$. In the anion-radical ($H_2C{=}CH^{-\bullet}$–CH_2SiMe_3), contribution of the acceptor effect within the σ*, π conjugation turns out in the foreground. As a result, the donor effect of the CH_2SiMe_3 substituent appears to be weaker and its $\sigma_R = -0.24$ decreases up to $\sigma_R = -0.11$.

Change in the nature of the substituent after the transformation of neutral molecules into the corresponding ion-radicals may be operative in the preparation of some unusual derivatives. One may transform an organic molecule into its ion-radical, change the substituent effect, perform the desired substitution, and after that, return the obtained system into the neutral state by the action of soft redox reactants.

1.2.2 Connections between Ion-Radical Reactivity and Electronic Structure of Ion-Radical Products

The reaction of aryl and hetaryl halides with the nitrile-stabilized carbanions ($RCH^{-}{-}CN$) leads to derivatives of ArCH(R)CN type. Sometimes, however, dimeric products of the type ArCH(R) CH(R)Ar are formed (Moon et al. 1983). As observed, 1-naphthyl, 2-pyridyl, and 2-quinolyl halides give the nitrile-substituted products, whereas phenyl halides, as a rule, form dimers. This is because of the manner of surplus electron localization in the anion-radical that arises on the replacement of the halogen by the nitrile-containing carbanion. If the resultant anion-radical contains an unpaired electron within the LUMO, covering mainly the aromatic ring, such an anion-radical is stable, with no inclination to split up. It is oxidized by the initial substrate and gives the final product in the neutral form: $[Ar]^{-\bullet}CH(R)CN - e \rightarrow ArCH(R)CN$. If the anion-radical formed acquires an unpaired electron on the CN group orbital, this group easily splits off in the form of the cyanide ion. Therefore, the dimer is formed as the final product: $2PhCH(R)[CN]^{-\bullet} \rightarrow 2CN^{-} + PhCH(R)CH(R)$.

One-electron reduction of organyl halides often results in the elimination of halide and the formation of organyl radicals: $RX + e \rightarrow RX^{-\bullet} \rightarrow R^{\bullet} + X^{-}$. The organyl radicals resulting in this cleavage can combine with the nucleophile anion: $R^{\bullet} + Y^{-} \rightarrow RY^{-\bullet}$. The anion-radical of this substituted product initiates a chain-reaction network: $RY^{-\bullet} + RX \rightarrow RY + RX^{-\bullet}$, and so on. According to Saveant (1994), an important contribution to the overall efficiency of this substitution reaction is given by the step in which $RY^{-\bullet}$ anion-radical is formed. In this step, an intramolecular electron-transfer or bond-forming process occurs when the nucleophile Y^{-} attacking the radical $R^{\bullet}$ begins to form the new species, characterized by an elongated two-center three-electron C∴Y bond. An unpaired electron in this anion-radical is at first allocated on a "low-energy" $\sigma_{C-Y}{}^{*}$ MO. With the progress of the formation of the C–Y bond, the energy of the σ* MO increases sharply until a changeover occurs. If R is Ar, the π* MO of the molecule becomes the LUMO. An internal transfer of the odd electron to the LUMO then takes place. Therefore, it follows that the substitution under consideration will be easier when the energy of the π* MO available in the $ArY^{-\bullet}$ species is lower. Papers by Rossi et al. (1994), Galli et al. (1995), and Borosky et al. (2000) have again underlined the following rule: The lower the energy of the LUMO of the $RY^{-\bullet}$ ($ArY^{-\bullet}$) species, the easier (faster) the reaction between $R^{\bullet}$ ($Ar^{\bullet}$) and Y^{-}.

It is worth noting, however, that the primary halide-containing anion-radicals may be somewhat stable if an aromatic molecule has another electron-acceptor group as a substituent such as the

nitro, cyano (Lawless et al. 1969), carbonyl (Bartak et al. 1973), or pyridinyl group (Neta and Behar 1981). In these cases, dehalogenation reactions proceed as intramolecular electron transfers from the groups $NO_2^{-\bullet}$ and $CN^{-\bullet}$ through the conjugated π system to the carbon–halogen fragment orbital. After that, the halide ion is eliminated. The splitting rate depends on the halogen nature (I > Br > Cl) and on the position of the halogen with respect to another substituent (ortho > para > meta) (Alwair and Grimshaw 1973, Neta and Behar 1981, Behar and Neta 1981, Galli 1988). The cleavage proceeds more easily at those positions that bear the maximal spin density. Change of the nitro group to the nitrile or carboxymethyl group leads to some facilitation of halogen elimination: A greater portion of spin density reaches the carbon–halogen orbital and the rate of dehalogenation increases.

For instance, the anion-radical of 4-fluoronitrobenzene is characterized with the a^F HFC constant of 0.855 mT and high stability (Starichenko et al. 1981). In contrast, the anion-radical of 4-fluorobenzonitrile has a significantly larger a^F HFC constant of 2.296 mT and readily cleaves in two particles, the benzonitrile σ radical and the fluoride ion (Buick et al. 1969). Comparison of these anion-radicals with respect to their C_{Ar}–F dissociation could be especially interesting in a medium capable of forming a hydrogen bond with the fluorine substituent. In the literature, the observed threefold lowering (rather than increasing) of a^F HFC constant in isopropanol is ascribed to the H bond formation between the fluorine in aromatic ring and the hydroxyl hydrogen of the alcohol (Rakitin et al. 2003). A comprehensive and systematic theoretical analysis confirms the ability of aromatic carbon–bound fluorine to engage in a hydrogen bond with a proton donor solvent (Razgulin and Mecozzi 2006).

It should be emphasized that the cause of halide mobility in aromatic anion-radical substitution is quite opposite to that in heterolytic aromatic substitution at the carbon-halogen bond. In anion-radicals, the carbon–halogen bond is enriched with electron density and after halide-ion expulsion an aromatic σ radical is formed. In neutral molecules, the carbon–halogen bond conjugated with an acceptor group becomes poor with respect to its electron density; a nucleophile attacks a carbon atom bearing a partial positive charge. Some kind of π binding was established between the nitro group and chlorine through the benzene ring in 4-nitrochlorobenzene (Geer and Byker 1982). As a result, the inductive effect of chlorine becomes suppressed in the neutral molecule. In the anion-radical, LUMO populated by one electron comes into operation. The HOMO role turns out to be insignificant. In anion-radicals, this orbital can cause only a slight disturbance. The negative charge, to a significant degree, moves into the benzene ring, and this movement is enforced at the expense of the chlorine-inductive effect. The carbon–chlorine bond is enriched with an electron. Eventually, Cl^- leaves the anion-radical species. The considered event is quite simple and its simplicity is based on the π-electron character of HOMO and LUMO.

However, there are some cases when an unpaired electron is localized not on the π, but on the σ orbital of an anion-radical. Of course, in such a case, a simple molecular orbital consideration that is based on the π approach does not coincide with experimental data. Chlorobenzothiadiazole may serve as a representative example (Gul'maliev et al. 1975). Although the thiadiazole ring is a weaker acceptor than the nitro group, the elimination of the chloride ion from the 5-chlorobenzothiadiazole anion-radical does not take place (Solodovnikov and Todres 1968). At the same time, the anion-radical of 7-chloroquinoline readily loses the chlorine anion (Fujinaga et al. 1968). Notably, 7-chloroquinoline is very close to 5-chlorobenzothiadiazole in the sense of structure and electrophilicity of the heterocycle. To explain the mentioned difference, calculations are needed to clearly take into account the σ electron framework of the molecules compared. It would also be interesting to exploit the concept of an increased valency in the consideration of anion-radical electronic structures, especially of those anion-radicals that contain atoms (fragments) with available *d* orbitals. This concept is traditionally derived from valence-shell expansion through the use of *d* orbital, but it is also understandable in terms of simple (and cheaper for calculations) MO theory, without *d*-orbital participation. For a comparative analysis refer the paper by ElSolhy et al. (2005). Solvation of intermediary states on the way to a final product should be involved in the calculations as well (Parker 1981).

Alkyl halide anion-radicals do not have π systems entirely. Nevertheless, they are able to exist in solutions. The potential barrier for the C—Cl cleavage is estimated to be ca. 70 kJ mol^{-1} (Abeywickrema and Della 1981, Eberson 1982). The carbon–halogen bond may capture one electron directly (Casado et al. 1987, Boorshtein and Gherman 1988).

It is interesting to compare SCl and SCN in relation to NO_2 as a reference group. Aryl sulfenyl chlorides and thiocyanates were subjected to two independent model-reductive cleavage reactions by treatment with (a) cyclooctatetraene dipotassium ($C_8H_8K_2$) in tetrahydrofuran (THF) or (b) $HSiCl_3$ + R_3N (R = alkyl) in benzene (Todres and Avagyan 1972, 1978). As established, aromatic sulfenyl chlorides under conditions a and b produce disulfides or thiols; the presence of the nitro group in the ring does not affect the reaction. Aryl thiocyanates without the nitro group behave in a similar way. However, aryl thiocyanates that contain the nitro group in the ring are converted into anion-radicals with the SCN remaining unchanged: $O_2NC_6H_4SCN + ½C_8H_8K_2 \rightarrow ½C_8H_8 + NCSC_6H_4NO_2^{-\bullet} K^+$.

Splitting of the SCN group is not observed and, after the one-electron oxidation, the initial $NCSC_6H_4NO_2^{-\bullet}$ anion-radical produces $NCSC_6H_4NO_2$. The recoveries are close to quantitative; disulfides and thiols are not observed. The thiocyanate group (SCN) thus competes less successfully with the nitro group (NO_2) for the extra electron than the sulfenyl chloride group (SCl).

The conclusion outlined earlier was entirely confirmed by quantum-chemical calculations. The results of the calculations are shown in Table 1.2 (LCAO MO CNDO/2 approach, see Todres et al. 1982).

As observed from Table 1.2, the SCl-group charge slightly depends on whether or not the NO_2 group is present in the benzene ring. In the case of thiocyanate anion-radicals, the charge on the SCN group is diminished by 50% if the NO_2 group is present in the molecule. Thus, SCl and SCN have different electron-attraction properties. This conclusion was not predictable *a priori*. Until recently, the extent of polarization in the SCl group has been considered to be comparable to that in the SCN group, according to the $S^{\delta+}—X^{\delta-}$ scheme. For instance, Kharash et al. (1953) have pointed out that nitroaryl thiocyanates as well as nitroaryl sulfenyl chlorides, when dissolved in concentrated sulfuric acid, are converted into the same nitroaryl sulfenium ions, O_2NArS^+. However, these findings indicate otherwise.

Other pertinent examples include splitting of the anion-radicals from *p*-nitrophenyl methyl sulfone and *p*-cyanophenyl methyl sulfone (Pilard et al. 2001). The nitrophenyl species undergoes the preferential cleavage of Ar—S bond, whereas the cyanophenyl species expels both CN and CH_3SO_2 groups in the two parallel cleavage reactions. All of the examples show that foreseeing a splitting direction and extending it from one parent compound to another is risky, especially in organic chemistry of ion-radicals.

One interesting point emerges from the work of Mueller et al. (2003) on "electromers" of the tetramethylene ethane cation-radical. These electromers differ in the nature of singly occupied (and closely located) MOs. The two species are interconvertible with very similar yet distinct ultraviolet (UV) spectra. The authors noted: "One may want to describe this peculiar kind of isomerism by the

TABLE 1.2
Effective Charges (q_i) on R and SX Groups in *p*-$RC_6H_4SX^{-\bullet}$ Anion-Radicals (the Rest of the Charge, up to Unity, Is in the Benzene Rings)

R	SX	−qR	−qSX
H	SCl	0.05	0.78
NO_2	SCl	0.20	0.76
H	SCN	0.06	0.54
NO_2	SCN	0.48	0.27

term 'electromers' … or 'luminomers' (to highlight the fact that the HOMOs and the LUMOs correlate)." To prolong terminological refining, one may want to describe these isomers as "somomers" because of the difference in their single-occupied molecular orbitals (SOMOs). Electromers in organometallic chemistry means distinct species that differ mainly by the oxidation state of the metal. Typical examples are the one-electron oxidation products of divinylphenylene-bridged diruthenium complexes described by Maurer et al. (2006). As with pure-organic electromers, choosing the correct term is a matter of the future, but the phenomenon itself should be emphasized here.

1.2.3 Bridge-Effect Peculiarities

Reactivity of ion-radicals is obviously defined by the manner of the spin-density distribution. In bridged molecules, the part of the molecule that combines its two fragments can play the role of a barrier or a stretch of conjugation. The bridge can participate in direct polar conjugation. The bridge-dependent intramolecular electron transfer can proceed through a thermally activated hopping mechanism or via superexchange. Superexchange occurs when bridge orbitals are utilized solely as a coupling medium. It is usually achieved when the bridge is short. When the bridge is longer, bridge-assisted hopping dynamics prevails. Although superexchange and hopping follow different distance laws, both mechanisms can be operative. Lambert et al. (2002) presented the relevant examples. Because of the book-volume limitations, our discussion will be restricted with spin distribution in the bridge-connected ion-radicals. This is crucial for the ion-radical reactivity and for the design of molecular wires and organic metals.

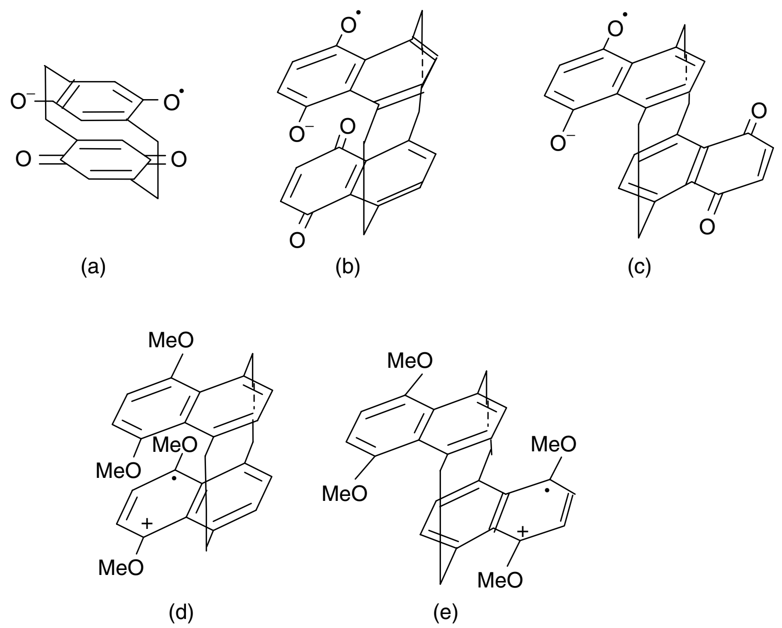
The bridged ion-radicals are usually subdivided into three classes (Robin and Day 1967, see also Dumur et al. 2004). Class I—the redox centers are completely localized and behave as separated entities, class II—intermediate coupling between the mixed-valence centers exists; class III—the redox centers are completely equivalent being enriched with an unpaired electron by the half-to-half manner. For instance, the cation-radical of *N*,*N*,*N*′,*N*′-tetraphenyl-*p*-phenylenediamine belongs to class III (Szeghalmi et al. 2004).

Let us now scrutinize ion-radicals of paracyclophanes. As the basis of our consideration, we chose the following species depicted in Schemes 1.4a through 1.4e and 1.5.

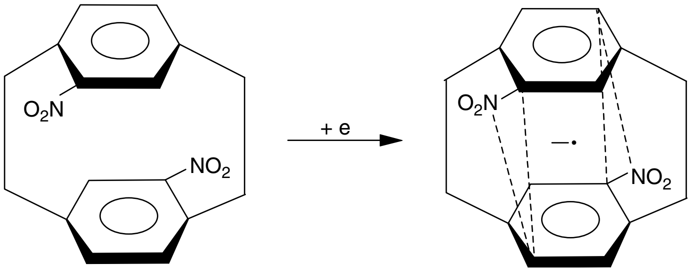
a. The anion-radical of *pseudogeminal*-[2.2]paracyclophane-4,7,12,15-tetrone in which the 1,4-benzoquinone units lie one beneath the other.
b. The anion-radical of *syn*-[2.2](1,4)naphthalenophane-4,7,14,17-tetrone in which there is the same spatial situation.
c. The anion-radical of *anti*-[2.2](1,4)naphthalenophane-4,7,12,15-tetrone in which the naphthoquinone units are further apart.
d. The cation-radical of *syn*-[2.2](1,4)naphthalenophane-4,7,14,17-tetramethoxy derivative, which is close to case b.
e. The cation-radical of *anti*-[2.2](1,4)naphthalenophane-4,7,14,17-tetramethoxy derivative, which resembles the case c structure.
f. The anion-radical of 5,11-*pseudopara*-dinitro-[2.2]paracylophane, which resembles the case a structure (Scheme 1.5).

As seen, cyclophane structures shown in Schemes 1.4b through 1.4e have the following unique feature: The through-bond distance within the paracyclophane fragment is held constant, whereas the spatial distance between the ion-radicalized and neutral moieties is changed. Therefore, the relative importance of through-bond and through-space mechanisms for intramolecular electron transfer can be learned directly from experimental data on these molecules.

All the compounds of Scheme 1.4 were examined for electrochemical reduction (cases a–c) or oxidation (cases d and e); two one-electron peak potentials were revealed with differences significantly higher than 20 mV (Wartini et al. 1998a, 1998b). A large difference between the first two



SCHEME 1.4



SCHEME 1.5

reduction or oxidation potentials is indicative of the delocalization of the first (unpaired) electron (Rak and Miller 1992). In other words, the two electrochemically active fragments can accept or lose a single electron, the second one-electron transfer being markedly hampered. In their turns, ESR and electron-nuclear double resonance (ENDOR) spectra of the anion-radicals under investigation gave evidence of delocalization of an unpaired electron over the whole molecule in each case. Because of the close spatial contact of the quinone units (0.31 nm between the centers of the 1,4-benzoquinone rings; Scheme 1.4a), one may suppose that the unpaired electron simply jumps over this narrow gap. If so, the whole-molecule delocalization would be impossible in the case of the mutual anti-arranged 1,4-naphthoquinone units (see Scheme 1.4c). However, this anti-arranged anion-radical shows the full spin-electron delocalization. Consequently, σ, π conjugation is realized in the anion-radicals of the paracyclophanes considered. This is the sense of bridge effect in the case described.

In the same way, the displacement of the unpaired electron over the whole molecules was observed for cation-radicals from Scheme 1.4d and 1.4e, in which 1,4-dimethoxynaphthalene units are syn- or anti-annealed to [2.2]paracyclophane (Wartini et al. 1998a, 1998b). In another study, the electron transfer between 1,4-dimethoxybenzene and 7,7-dicyanobenzoquinone methide moieties

in syn- or anti-cyclophane systems reached the same conclusion: The through-bond mechanism can remain the dominant reaction pathway at short donor–acceptor distances as well (Pullen et al. 1997).

Scheme 1.5 represents case f, that is, an anion-radical belonging to the borderline between moderately and completely delocalized species. Its optical spectra, along with frontier orbital analysis, testifies that in this anion-radical there is a positive overlap between C–N bonds and the pseudo-geminal carbons of the opposite rings, as shown by the dashed lines in the structure of Scheme 1.5 (Nelsen et al. 2005). Taken together, the experimental results considered provide direct evidence for the through-bond mechanism of electron transfer in these paracyclophane systems.

Other examples of the specified bridge effect deal with anion-radicals of aryl derivatives of the tricoordinated boron or tri- and five-coordinated phosphorus. In the tris(pentafluorophenyl)boran anion-radical, spin density is effectively transferred from the boron *p* orbital to an antibonding π MOs of the phenyl rings (Kwaan et al. 2001). Studies of the phosphorus-containing aromatic anion-radicals have been more informative. As known, phosphorus interrupts conjugation between aryl fragments in the corresponding neutral compounds. In contrast to the neutral molecules, the phosphorus atom transmits conjugation in Ar_3P and $Ar_3P(O)$ anion-radicals (Il'yasov et al. 1980). At least formally, the P atom appears to be a bridge, not a barrier. Perhaps, the phosphorus unfilled *p*- or *d* orbital takes part in this transmission effect. As with Ar_3P cation-radicals, there is an opinion (Tojo et al. 2006) that the positive charge of the phosphorus atom is delocalized in $Ar_3P^{+\bullet}$ because of the π-electron conjugation of the aromatic ring, whereas an unpaired electron is localized on the phosphorus atom. Note that the highest-occupied orbital of Ar_3P is the nonbonding orbital (n orbital) of the phosphorus atom (Culcasi et al. 1991). As early as in 1975, it had been predicted that the unpaired electron should be localized on the phosphorus atom (Berclaz and Geoffroy 1975). The situation just described has, of course, some peculiarities for other phosphine derivatives. The cation-radical $[P(OMe/OEt)_3]^{+\bullet}$ contains an unpaired electron predominantly on the phosphorus atom, which facilitates the radical coupling of this cation-radical with the $Ar^\bullet$ radical from aryl diazonium salts. In $[PhP(OMe/OEt)_2]^{+\bullet}$ and $[Ph_2P(OMe/OEt)]^{+\bullet}$ cation-radicals, an unpaired electron is somewhat shifted from the phosphorus atom to the phenyl ring(s). This reduces the spin density at the central phosphorus atoms, making the reaction of the mentioned cation-radicals with $Ar^\bullet$ slower (Yasui et al. 1994a, 1994b). Similar to the cation-radicals, the phosphoranyl radicals with and without the aryl ligand(s) exhibit small and large values of phosphorus HFC constants, respectively, in the ESR spectra (Boekenstein et al. 1974; Davies et al. 1974, 1976). This means that the unpaired electron is transferred to the aryl ligands of aryl alkyl phosphoranyl radicals also, but it is wholly held by the central phosphorus in the case of alkyl phosphoranyl radicals.

Tris(ferrocenyl)phosphine, Fc_3P, undergoes oxidations of each ferrocenyl moiety in three different steps. This means that there is the same through-bond charge delocalization, but with some participation of the phosphorus atom (Barriere et al. 2005).

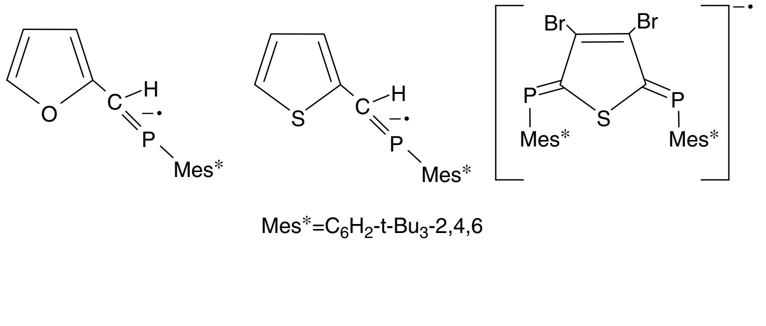
Peculiarities of the P=N bridge in cation-radicals were scrutinized by Sudhakar and Lammertsma (1991), Guidi et al. (2005), and Matni et al. (2005). Considering conjugation in cation radicals containing bis(iminophosphorane) phenylene bridge, Matni et al. (2005) experimentally (anodic oxidation in the ESR resonator) and theoretically (B3LYP method of density functional theory [DFT]) studied the para, ortho, and meta isomers of the general formula $R_3P{=}NC_6H_4N{=}PR_3$, where R constitutes Ph in the experiments and H in the calculations. An appreciable spin density was observed on the nitrogen atom of each P=N bond. The remaining part is delocalized on the central phenylene ring that served as a bridge between the two iminophosphoranyl groups. The spin-density distribution in the phenylene ring depends on the type of its substitution, that is, para, ortho, and meta. Such distribution plays a crucial role in the cation-radical stability. For example, oxidation of the parent iminophosphorane is reversible for para, pseudoreversible for ortho, and irreversible for meta. The para cation-radical appeared to be persistent: It can be detected through the resolved ESR spectrum even 4 h after the voltage has been switched off. The ortho cation-radical showed the resolved ESR spectrum when anodic current was passed. Absolutely no ESR signal could be detected for the meta isomer.

Let us now direct our attention to the P=C bond in phosphaalkene ion-radicals. The literature contains data on two such anion-radicals in which a furan and a thiophene ring are bound to the carbon atom, and the 2,4,6-tri(*tert*-butyl)phenyl group is bound to the phosphorus atom. According to the ESR spectra of anion-radicals, an unpaired electron is delocalized on a π* orbital built from the five-membered ring (furanyl or thienyl) and the P=C bond. The participation of the phosphaalkene moiety in this MO was estimated at about 60% and some moderate (but sufficient) transmission of the spin density occurs through the P=C bridge (Jouaiti et al. 1997). Scheme 1.6 depicts the structures under discussion.

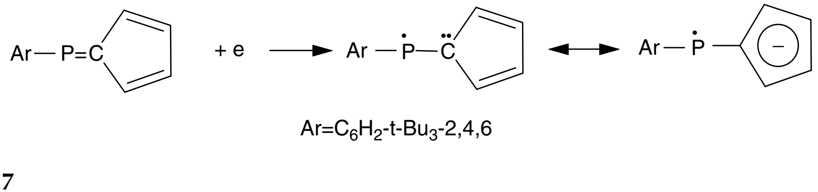
The anion-radical from dibromodiphosphathienoquinone is also included in Scheme 1.6. According to the ESR spectrum of this anion-radical potassium salt in THF, both the phosphorus atoms bear spin density. It is worth noting that the corresponding HFC constants are nonequivalent; a(P1) = 9.3 mT, whereas a(P2) = 2.1 mT Murakami et al. (2002). Such a difference may be caused by an ion-pair formation with the potassium cation. Ward (1961) had noted the same difference for the potassium salt of the *p*-dinitrobenzene anion-radical where a(N1) was more than a(N2). Importantly, Ward had observed a(N1) = a(N2) when tetraalkylammonium rather than potassium was the counterion. It is obvious that the nitro groups in the *p*-dinitrobenzene anion-radical are completely conjugated through the ring π system. However, ion pairing with K^+ really forced the two nitro groups to be nonequivalent in the *p*-dinitrobenzene anion-radical. Owing to steric hindrance, the ion pair with Alk_4N^+ cannot be so strong and both the nitro groups in the *p*-dinitrobenzene anion-radical appear to be equivalent. It would be interesting to compare a(P1) and a(P2) for the dibromodiphosphathienoquinone having not the potassium but tetraalkylammonium counterion.

If the carbon atom of the P=C bond is an integral part of the cyclopentadiene ring, the unpaired electron distribution proceeds in the way of spin-charge scattering (Al Badri et al. 1997). Scheme 1.7 illustrates this special case.

Hence, the possibility to acquire aromaticity (conferred by the presence of six π electrons in the five-carbon-membered ring) considerably increases the electron affinity of this ring. As a result, one of the two π electrons of the P=C bond remains on the phosphorus atom, and the other combines with the excess electron to create the cyclopentadienyl π-electron sextet. The situation is analogous to that in the diphenylfulvene anion-radical as analyzed in Chapter 3 (see Section 3.2.2).



SCHEME 1.6



SCHEME 1.7

The anion-radical of the bis(phosphaalkene) containing the phenyl ring linked to the phosphorus atoms gives another aspect of the bridge effect. The unpaired electron is delocalized in this anion-radical on both the P=C bond and the phenyl ring (Geoffroy et al. 1992). Probably, the C=P–C_6H_4–P=C fragment adopts a quinoidal structure, Mes*$C^{(\bullet)}$–P=C_6H_4=P–$C^{(-)}$Mes* ↔ Mes*$C^{(-)}$–P=C_6H_4=P–$C^{(\bullet)}$Mes* (Al Badri et al. 1999, Dutan et al. 2003). The ESR spectrum points out to delocalization of an unpaired electron through the whole phosphaquinoid skeleton with limited spin density in the central ring (Sasaki et al. 1999, Murakami et al. 2005).

Diphosphaallene derivatives ArP=C=PAr are peculiar compounds because of the presence of the two orthogonal carbon–phosphorus double bonds. The compounds were transformed into cation-radicals on electrochemical or chemical one-electron oxidation. As found, the unpaired electron is located on an MO constituted mainly by a *p* orbital of each phosphorus atom and a *p* orbital of the carbon atom (Chentit et al. 1997, Alberti et al. 1999).

On electrochemical or chemical reduction, aromatic phosphaallene derivatives yield anion-radicals. These species have two equivalent phosphorus nuclei. The unpaired electron oscillates between the two phosphorus atoms (Sidorenkova et al. 1998, Alberti et al. 1999): ArP=C($^-$)−P($^\bullet$)Ar ↔ ArP($^\bullet$)−C($^-$)=PAr.

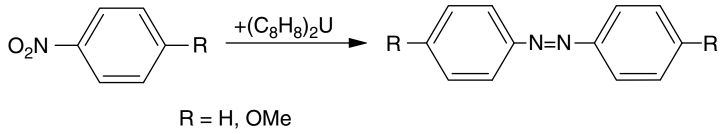
Consequently, the electron structures of the diphosphaallene ion-radicals resemble those of the allene ion-radicals where the allenic fragment works as a bridge for conjugation (see Section 3.3.2). Interestingly, in the anion-radical, a spin density on the phosphorus atom is higher than that in the cation-radical. In the anion-radical, the SOMO is seemingly formed at the expense of vacant and low-lying *d* or *f* orbitals of phosphorus, whereas in the cation-radical, the SOMO originates from the neighboring occupied orbitals of phosphorus and carbon. For both the ion-radicals, the existence of cis- and trans-geometrical isomers were predicted by B3LYP calculation, the trans-isomer being more stable. The trans-ion-radical supposedly has a planar structure. In other words, the one-electron transfer causes definite flattening of the parent molecule in the same way as it is observed in the case of allenes.

In the case of $[ArP{=}C(NMe_2)_2]^{+\bullet}$, the dimethylamino groups naturally localize the hole at their nodal carbon atom, whereas the spin is detained by the phosphorus atom, namely, $ArP^{\bullet}{-}[C(NMe_2)]^{+}$ (Rosa et al. 2003).

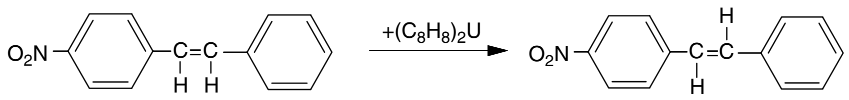
Let us now consider the role of P=P bridge in the anion-radicals of diaryldiphosphenes, $[ArP{=}PAr]^{-\bullet}$. Sasamori et al. (2006a, 2006b) prepared kinetically stable anion-radicals of this type, reducing a parent diaryldiphosphene bearing a bulky substituent in the aryl rings. According to the electrochemical and ESR spectral data alongside the results of DFT calculations, the introduction of one electron leads to the population of the antibonding π* orbital of the P=P double bond with some participation of the aryl moieties.

Having this result in mind, it is interesting to scrutinize the role of the C=C bridge in ArCH=CHAr′ derivatives. This bridge is good at transmitting conjugation in neutral stilbenes, but in stilbene anion-radicals it can also operate as a hollow on the conjugation route. At first glance, the unpaired electron distribution in the nitrostilbene anion-radical has to be similar to that in the nitrobenzene anion-radical. The consensus is that the LUMO of neutral aromatic nitro derivatives (the orbital that accommodates the electron introduced) is essentially an orbital of the "free" nitro group. The styryl fragment of neutral 4-nitrostilbene is conjugated with the nitro group and acts as a weak donor. This is indicated by values of the Hammett constants: $\sigma_p(NO_2C_6H_4-)$ is +0.23 and σ_p(−CH=CHPh) is −0.07.

If the styryl substituent retained its donor nature in the anion-radical state, an increase, not a decrease in the value of the nitrogen HFC constant (*a*(N)) would have been observed. Experiments show that *a*(N) values for anion-radicals of nitrostilbenes decrease (not increase) in comparison with the *a*(N) value for the anion-radical of nitrobenzene (Todres 1992). Both "naked" anion-radicals and anion-radicals involved in forming complexes with the potassium cations obey such regularity. In the cases of potassium complexes with THF as a solvent, *a*(N) = 0.980 mT for $PhNO_2$ anion-radical and *a*(N) = 0.890 mT for PhCH=$CHC_6H_4NO_2$-4 anion-radical. In the presence of 18-crown-6-ether



SCHEME 1.8



SCHEME 1.9

as a decomplexing agent in THF solution, a(N) = 0.848 mT for $PhNO_2$ anion-radical and a(N) = 0.680 mT for $PhCH{=}CHC_6H_4NO_2$-2 anion-radical.

Reduction of nitrobenzene (Grant and Streitwieser 1978, Todres et al. 1985) and 4-methoxy-nitrobenzene (Todres et al. 1985) by uranium, thorium, and lanthanum–di(cyclooctatetraene) complexes leads to azo compounds. Scheme 1.8 illustrates these reductive reactions using the di(cyclooctatetraene)–uranium complex as an example.

Under the same conditions, 4-styryl nitrobenzene (4-nitrostilbene) undergoes cis-to-trans isomerization only, with no changes in the nitro group (Todres et al. 1984, 1985; Scheme 1.9).

Thus, it appears that the focal point of the reaction has been transferred. The presence of a styryl (not a methoxyl) group protects the nitro group from being reduced. For some reason, the styryl group causes a shift of excess electron density from the nitro to the ethylene fragment. This subtle difference between the anion-radicals of nitrobenzene and nitrostilbene, observed experimentally, is well reproduced by quantum-chemical calculations (Todres et al. 1984). Single-electron wave-function analysis of the vacant orbitals in both the molecules shows that one-electron reduction of *cis*-4-nitrostilbene must be accompanied by the predominant localization of an upaired electron in the region of the ethylene moiety. Participation of the nitro group atomic orbitals appears to be insignificant. The nitro group atomic coefficients in the molecular wave function for *cis*-4-nitrostilbene are half of that for nitrobenzene. The excess electron population (q) of the first vacant orbital for the nitro groups is 0.3832 for the nitrobenzene anion-radical and 0.0764 for the nitrostilbene anion-radical. The unpaired electron is localized largely on the ethylene fragment of the nitrostilbene skeleton (q = 0.2629). Moreover, the first vacant level of the *cis*-4-nitrostilbene molecule has lower energy than that of the nitrobenzene molecule: 38 and 135 kJ, respectively.

This means that 4-nitrostilbene is a more effective electron acceptor than nitrobenzene. This theoretical conclusion is verified by experiments. The charge-transfer complexes formed by nitrobenzene or 4-nitrostilbene with *N*,*N*-dimethylaniline have stability constants of 0.085 L mol^{-1} or 0.296 L mol^{-1}, respectively. Moreover, the formation of the charge-transfer complex between *cis*-4-nitrostilbene and *N*,*N*-dimethylaniline indeed results in cis-to-trans conversion (Dyusengaliev et al. 1995). This conversion proceeds slowly in the charge-transfer complex, but runs rapidly after one-electron transfer leading to the nitrostilbene anion-radical (Todres 1992). The cis–trans conversion of ion-radicals will be considered in detail later. (see sections 3.2.5.1, 6.4, and 8.2.1).

It is interesting to compare the fate of the C=C bridge in the anion-radicals of 4-nitrostilbene (Todres 1990) with 4-acetyl-α,β-diphenylstilbene (Wolf et al. 1996). When treated with potassium or sodium in THF and then with water, neutral 4-nitrostilbene does not undergo a multi-electron reduction of the nitro group or the C=C bridge. Under the same conditions, 4-acetyl-α,β-diphenylstilbene produces a pinacol, $[Ph_2C{=}C(Ph)C_6H_4C(OH)CH_3]_2$. As calculations show, the carbonyl of the acetyl group in 4-acetyl-α,β-diphenylstilbene is the site of significant reduction. The formal charge on the carbonyl carbon and oxygen atoms become significantly more negative on addition of one electron,

whereas the olefinic carbons become only slightly more negative (Wolf et al. 1996). It is worth pointing out that the phenylcarbonyl group is a stronger acceptor than the nitrophenyl group: $\sigma_p(-COC_6H_5) = +0.46(\sigma_p(-COCH_3) = +0.52)$, whereas $\sigma_p(NO_2C_6H_4-) = +0.23(\sigma_p(-NO_2) = +0.78)$. In addition, the phenylacetyl group in the molecule under consideration is conjugated only slightly, if at all, with the C=C bridge because this molecule is propeller shaped (Hoekstra and Vos 1975). Although the acetyl group is situated in the plane of the phenyl ring attached to it, it remains separated from the C=C bridge.

In contrast, the nitro and ethylenic fragments in *trans*-4-nitrostilbene form the united conjugation system. Such a conjugation is a necessary condition for the whole-contour delocalization of an unpaired electron in arylethylene anion-radicals. Whether this condition is the only one or there is some interval of allowable strength for the acceptor is a question left to future experiments.

1.3 ACID–BASE PROPERTIES OF ORGANIC ION-RADICALS

1.3.1 Anion-Radicals

Let us compare anion-radicals with dianions, which are definitely stronger bases. For example, the cyclooctatetraene dianion ($C_8H_8^{2-}$) accepts protons even from solvents such as dimethylsulfoxide (DMSO) and *N*,*N*-dimethylformamide. The latter is traditionally qualified as an aprotic solvent. In this solvent, the cyclooctatetraene dianion undergoes protonation resulting in the formation of cyclooctatrienes (Allendoerfer and Rieger 1965): $C_8H_8^{2-} + 2H^+ \rightarrow C_8H_{10}$. It is seen that $C_8H_8^{2-}$, with two introduced electrons, is essentially the counterpart or aprotic equivalent, or base, of the corresponding C-H acid.

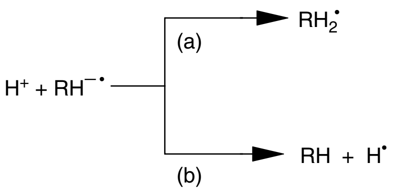
1.3.1.1 Anion-Radical Basicity

Having only one excess electron, anion-radicals can be considered as aprotic "half-equivalents" of the corresponding C-H acids. Reacting with protons, anion-radicals display some dual behavior. As a base, an anion-radical can add a proton, get rid off its negative charge, and give a radical. This reaction is represented by direction a in Scheme 1.10. As a radical, an anion-radical may generate atomic hydrogen from an alighting proton and transform into a parent uncharged compound according to direction b in Scheme 1.10.

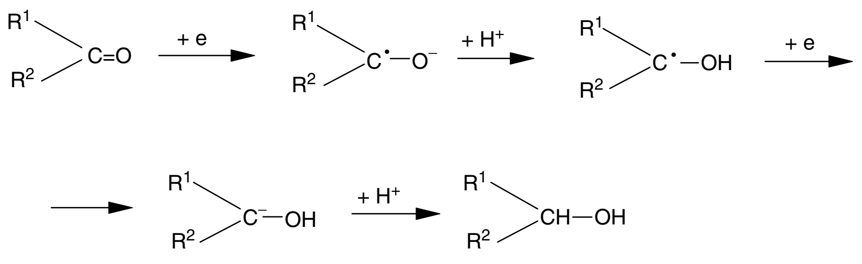
Such a dual reactivity toward protons depends on the difference between proton affinity to an electron and the first ionization potential of an anion-radical. This difference may not be very strong. The fate of the competition between directions a and b in Scheme 1.10 also depends on relative stability of the reaction products. It is reasonable to illustrate the duality with two extreme examples from real synthetic practice.

Direction a. Alkali metals transform saturated ketones into secondary alcohols. The reaction proceeds in the mixture of ethanol and liquid ammonia in the presence of ammonium chloride as a proton donor and follows Scheme 1.11 (Rautenstrauch et al. 1981).

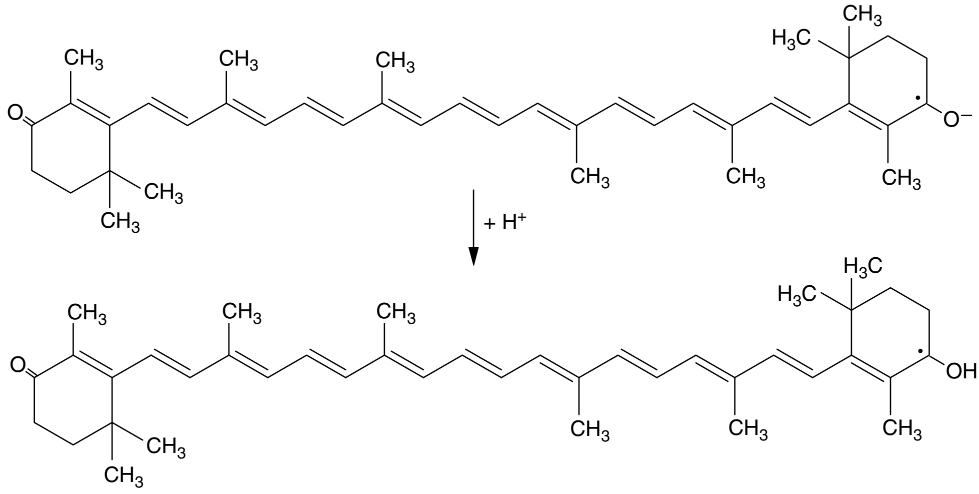
Scheme 1.12 gives another example of $C^\bullet$—O^- protonation, in this case of the canthaxantin, a biologically important carotenoid (El-Agamey et al. 2006, Edge et al. 2007).



SCHEME 1.10



SCHEME 1.11



SCHEME 1.12

Controlled one-electron reductions transform 1,2,3,4-tetraphenyl-1,3-cyclopentadiene or 1,2,3,4,5-pentaphenyl-1,3-cyclopentadiene into mixtures of the dihydrogenated products and the corresponding cyclopentadienyl anions (Farnia et al. 1999). The anion-radicals initially formed are protonated by the substrates themselves. The latter are thermodynamically very strong acids because of their strong tendency to aromatization. As with the cyclopentadiene anion-radicals, they need two protons to give more or less stable cyclopentadienes. The following equations represent the initial one-electron electrode reduction of 1,2,3,4,5-pentaphenyl-1,3-cyclopentadiene (C_5HAr_5) and explains the ratio and the nature of the products obtained at the expense of the further reactions in the electrolytic pool:

$$C_5H(Ar)_5 + e \rightarrow [C_5H(Ar)_5]^{-\bullet}$$

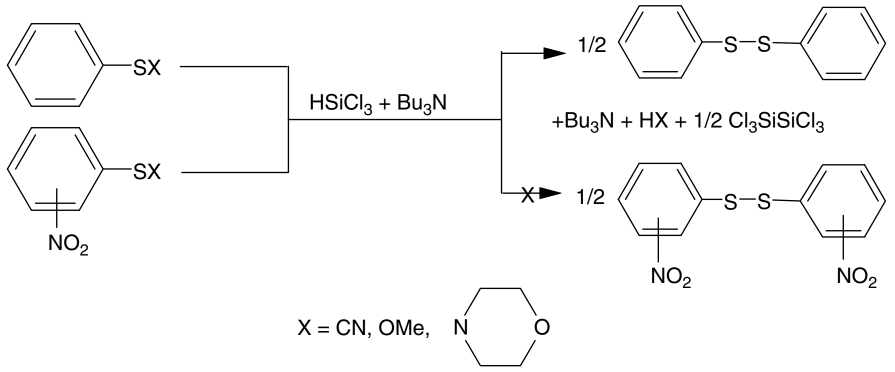
$$[C_5H(Ar)_5]^{-\bullet} + C_5H(Ar)_5 \rightarrow [C_5H_2(Ar)_5]^{\bullet} + [C_5(Ar)_5]^{-}$$

$$[C_5H_2(Ar)_5]^{\bullet} + [C_5H(Ar)_5]^{-\bullet} \rightarrow [C_5H_2(Ar)_5]^{-} + C_5H(Ar)_5$$

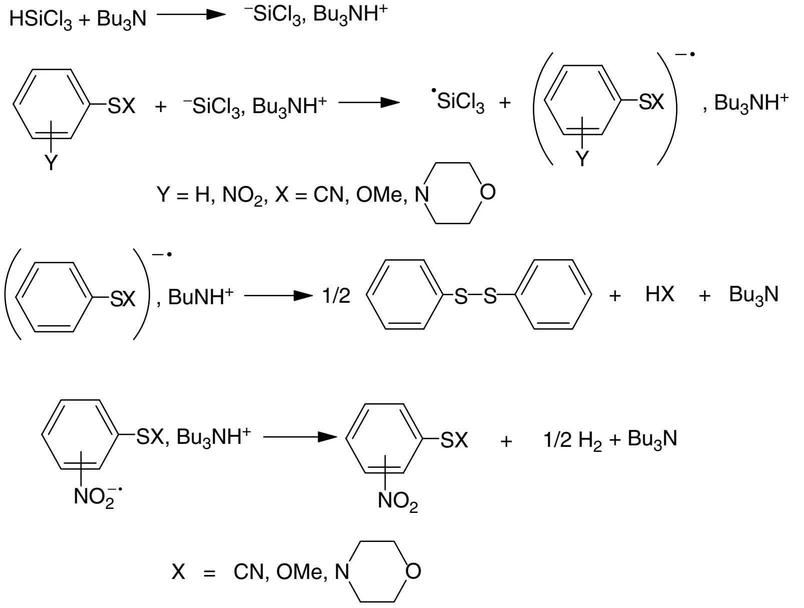
$$[C_5H_2(Ar)_5]^{-} + C_5H(Ar)_5 \rightarrow C_5H_3(Ar)_5 + [C_5(Ar)_5]^{-}$$

On the whole, $C_5H(Ar)_5 + 2[C_5H(Ar)_5]^{-\bullet} \rightarrow C_5H_3(Ar)_5 + 2[C_5(Ar)_5]^{-}$.

Hence, the case represents a typical example of the so-called father–son self-protonation process, provoked by the partial transformation of cyclopentadiene into the anion-radical.



SCHEME 1.13



SCHEME 1.14

Direction b of Scheme 1.10. The mixture of trichlorosilane and tributylamine in benzene reduces organic derivatives of two-valence sulfur such as benzene sulfenates. However, nitrobenzene sulfenates remain intact in this system (Todres and Avagyan 1978; Scheme 1.13).

Introduction of nitrobenzene sulfenates into the same mixture of trichlorosilane and tributylamine results in the evolution of hydrogen. As proven by Todres and Avagyan (1978), trichlorosilane with tributylamine yields the trichlorosilyl anion and tributylammonium cation. This stage starts the process involving one-electron transfer from the anion to a nitrobenzene sulfenate. At that time, nitrobenzene sulfenate produces the stable anion-radical with the tributylammonium counterion. The anion-radical gives off an unpaired electron to the proton from the counterion (see Scheme 1.14).

Returning to direction a in Scheme 1.10, it is interesting to compare pK_a values of protonated aromatic anion-radicals, $pK_a(ArH_2^{\bullet})$ and pK_a values of parent aromatics protonated in the absence of a preliminary electron transfer, $pK_a(ArH_2)$. As seen from Table 1.3, if the anion-radicals accept a proton, they hold it much more firmly than the parental neutral molecules (ΔpK_a values are positive).

TABLE 1.3
Differences in pK_a Values between Protonated Aromatic Compounds and Protonated Forms of the Anion-Radicals

ArH	pK_a(ArH_2^+)	pK_a($ArH_2^\bullet$)	ΔpK_a
Benzene	−23	>13.5	>36
NO_2-benzene	−11.3	3.2	14.5
Benzonitrile	−10.4	7.3	17.7
p-Me-benzoate	−7.8	5.5	13.3
Benzaldehyde	−7.1	8.4–10.5	15.5–17.6
Fluorenone	−6.6	6.3	12.9
Benzophenone	−6.2	9.2	15.4
Acetophenone	−6.2	9.9	16.1
Benzamide	−1.9	7.7	9.6
Benzoate	4.2	12.0	7.8

Source: Bil'kis, I.I. and Shteingarts, V.D. *Izv. SO AN SSSR, Ser. Khim. Nauk*, 105, 1987.

Contrary to the early indications (Kalsbeck and Thorp 1994), the anion-radical of C_{60} fullerene is a very weak base. This conclusion stems from a review by Reed and Bolskar (2000). In *o*-dichlorobenzene, the acidity of $C_{60}H^\bullet$ approaches that of dilute triflic acid. In DMSO, the pK_a of $C_{60}H^\bullet$ is estimated to be about nine, making it a slightly weaker acid than *p*-benzoic acid. These data are consistent with the reports that the ESR spectrum of $C_{60}^{-\bullet}$ remains practically invariable in the presence of water. There are aryl and methyl derivatives of $C_{60}^{-\bullet}$ that are stable and soluble in water (Sawamura et al. 2000). The weak basicity of $C_{60}^{-\bullet}$ is due to its intrinsically high stability through delocalization of the negative charge toward the 50π-electron system. When $C_{60}H^\bullet$ comes up, it formally produces a carbon radical α to the site of protonation, and the energetic cost of this localization is high. There is no electrochemical evidence for the reasonable expectation of dimerization of $C_{60}H^\bullet$ radicals (Cliffel and Bard 1994).

Proton landing defines the basicity of anion-radicals. This landing assumes 1:1 stoichiometry with respect to an anion-radical and a proton donor molecule. For example, in the reaction of the naphthalene anion-radical ($C_{10}H_8^{-\bullet}$) with methanol, this 1:1 stoichiometry should result in the formation of 50:50% mixture of naphthalene ($C_{10}H_8$) and dihydronaphthalene ($C_{10}H_{10}$).

$$C_{10}H_8^{-\bullet} + H^+ \rightarrow C_{10}H_9^\bullet$$

$$C_{10}H_9^\bullet + C_{10}H_8^{-\bullet} \rightarrow C_{10}H_9^- + C_{10}H_8$$

$$C_{10}H_9^- + H^+ \rightarrow C_{10}H_{10}$$

On the whole, $2C_{10}H_8^{-\bullet} + 2H^+ \rightarrow C_{10}H_8 + C_{10}H_{10}$.

Surprisingly, Screttas et al. (1996) have found that the reaction of the lithium naphthalene anion-radical with methanol in THF follows the 2:1 stoichiometry and leads to the $C_{10}H_8$–$C_{10}H_{10}$ mixture in the 95:5 ratio. The authors proposed the following alternative:

$$C_{10}H_8^{-\bullet}Li^+ + MeOH \rightarrow C_{10}H_9^\bullet + MeOLi$$

$$C_{10}H_9^\bullet + C_{10}H_8^{-\bullet}Li^+ \rightarrow C_{10}H_9^-Li^+ + C_{10}H_8$$

$$C_{10}H_9^-Li^+ \rightarrow C_{10}H_8 + LiH$$

$$C_{10}H_9^-Li^+ + MeOH \rightarrow MeOLi + C_{10}H_{10}$$

$$LiH + MeOH \rightarrow MeOLi + H_2$$

The decisive point of the scheme of Screttas et al. (1996) is the metal-hydride elimination from $C_{10}H_9^-Li^+$. The authors admitted that the weakness of their scheme is the lack of evidence for the formation of alkali metal hydride and for the formation of H_2 from the (supposed) reaction between the protonating agent and the alkali metal hydride. However, the main sense of this scheme consists of its better agreement with the observed stoichiometry. Of course, the initial proton landing can have more intimate mechanism, for example, electron transfer from the anion-radical to the protonating agent, followed by a hydrogen atom attack on the neutral naphthalene and production of dihydronaphthyl radical intermediate as follows:

$$C_{10}H_8^{-\bullet}Li^+ + MeOH \rightarrow [C_{10}H_8^{-\bullet}Li^+, MeOH] \rightarrow [C_{10}H_8, Li^+MeO^-, H^\bullet]$$

$$[C_{10}H_8, Li^+MeO^-, H^\bullet] \rightarrow MeOLi + C_{10}H_9^\bullet$$

Alonso et al. (2005) described anion-radical proton abstraction from prochiral organic acids. If the anion radicals were formed from homochiral predecessors, asymmetric deprotonation can be reached. However, low reactivity of the anion radical is required: Slow proton transfer, that is, high activation energy of the reaction discriminates well between diastereoselective transition states.

1.3.1.2 Pathways of Hydrogen Detachment from Anion-Radicals

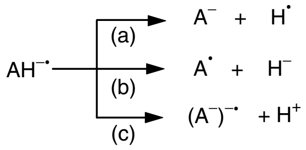
As a rule, the addition of an extra electron to a parent organic molecule leads to significant weakening of bonds in a forming anion-radical, thereby facilitating bond breaking. According to Zhao and Bordwell (1996a), there are three feasible different pathways of hydrogen detachment from anion-radicals ($AH^{-\bullet}$). These three pathways are compared in Scheme 1.15.

In Scheme 1.15, path a can be demonstrated with examples of anion-radicals of amino and hydroxy derivatives of 2,1,3-benzothiadiazole (Asfandiarov et al. 1998) and the azafullerene anion-radical, $C_{59}HN^{-\bullet}$ (Keshavarz et al. 1996). One of the examples, hydrogen atom detachment from $C_{59}HN^{-\bullet}$, is as follows:

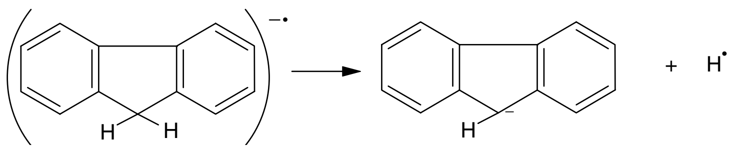
$$C_{59}HN^{-\bullet} \rightarrow C_{59}N^- + H^\bullet$$

Another example of path a of Scheme 1.15 is the anion-radical derived from fluorene. It undergoes a first-order decay to give the conjugate base (the fluorenide anion) and a hydrogen atom (Casson and Tabner 1969) according to Scheme 1.16.

Scheme 1.17 represents an anion-radical in which hydrogen abstraction is forced with the following two factors: The formation of the more stable bicyclical anion-radical and the elimination of



SCHEME 1.15



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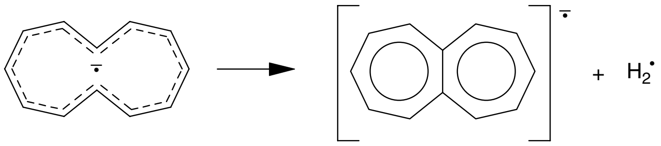
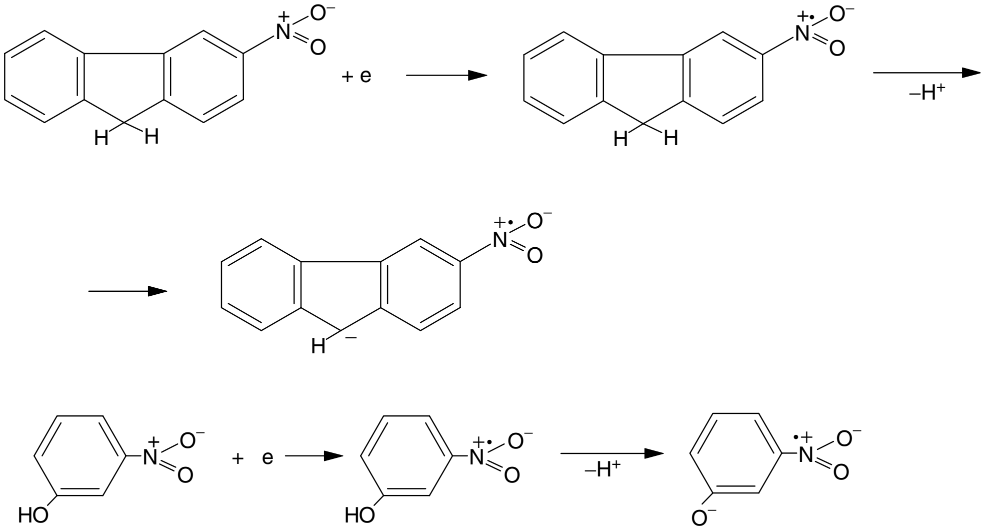


SCHEME 1.17



SCHEME 1.18

the stable molecule of dihydrogen spontaneously (Gard et al. 2004, Kiesewetter et al. 2006). This is a modification of path a of Scheme 1.15.

Path a of Scheme 1.15 has some kinetic preference since it can be linked with the strongly exothermic dimerization of the hydrogen atoms formed (Zhang and Bordwell 1992).

As with path b of Scheme 1.15, hydride loss from organic anion-radicals is generally not as favorable as the hydrogen atom loss because the solvation of the hydride ion and the organic anions is similar. Generally, path a of Scheme 1.15 is favored over path b in a wide set of organic anion-radicals. Free energies of bond dissociation for the anion-radicals to give a hydride ion and a radical by path b are the highest-energy pathways (Zhao and Bordwell 1996b).

In Scheme 1.15, path c is sometimes a feasible process. Thus, for the anion-radical derived from 4-nitrobenzyl cyanide, path c is favored over paths a and b by 84 and 150 kJ mol^{-1}, respectively. Typical examples of anion-radical deprotonation are the reactions in Scheme 1.18 (Zhao and Bordwell 1996a). It is path c of Scheme 1.15 that describes the acidity of anion-radicals,

TABLE 1.4
Differences in pK_a Values between Aromatic Weak Acids (RH) and Their Anion-Radicals ($RH^{-\bullet}$)

RH	pK_a(RH)	pK_a($RH^{-\bullet}$)	$-\Delta$pK_a
4-$NO_2C_6H_4OH$	10.8	21.0	10.2
3-$NO_2C_6H_4OH$	14.4	19.4	5.0
4-$NO_2C_6H_4SH$	5.5	15.5	10.0
4-$NO_2C_6H_4COOH$	9.0	13.6	4.6
4-$NO_2C_6H_4NHPh$	16.9	26.1	9.2
4-$NO_2C_6H_4CH_2CN$	12.3	23.4	11.1
3-$NO_2C_6H_4CH_2CN$	18.1	23.9	5.8
2-Nitrofluorene	17.0	24.7	7.7

Source: Zhao, Y. and Bordwell, F.G., *J. Org. Chem.*, 61, 2530, 1996a.

pK_a($RH^{-\bullet}$). Table 1.4 compares the pK_a values of nitro-substituted aromatic weak acids (RH) and their anion-radicals ($RH^{-\bullet}$) in DMSO.

Dianion-radicals formed in path c of Scheme 1.15 are inherently unstable species because they bear a double negative charge as well as an odd electron. The nitro group can exert an unusually stabilizing effect since it can fasten both a negative charge and an added electron. As seen from Table 1.4, the anion-radicals are less acidic than their parent compounds. One can expect such weakening in acidity owing to the combined action of two factors: The negative charge retards the loss of a proton, and the formed dianion-radical is inherently unstable.

One very unusual case of prototropic isomerization was revealed for anion-radicals of 1,4-dihydropyridine derivatives (Gavars et al. 1999). These anion-radicals transform into 4,5-dihydropyridine analogs through proton detachment and addition.

1.3.2 Cation-Radicals

Schmittel and Burghart (1997) had published a well-structured review on cation-radical chemistry. The review gave a general picture of the cation-radical nature compiling data of those days. This section scrutinizes data relevant to acid–base reactivity of organic ion-radicals.

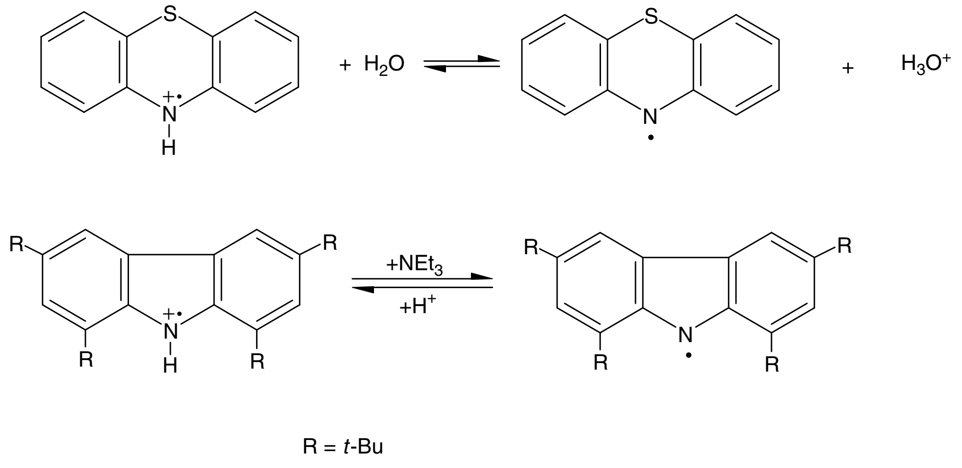
1.3.2.1 Cation-Radical Acidity

Deprotonation is a typical direction of cation-radical reactivity. Cation-radicals are usually strong H acids (e.g., the alkane cation-radicals pass its protons to the alcohol molecules; Sviridenko et al. 2001). Bases that conjugate with these H acids are radicals: $RH^{+\bullet} \rightarrow H^+ + R^\bullet$. Scheme 1.19 displays two real cases of this deprotonation (Neugebauer et al. 1972).

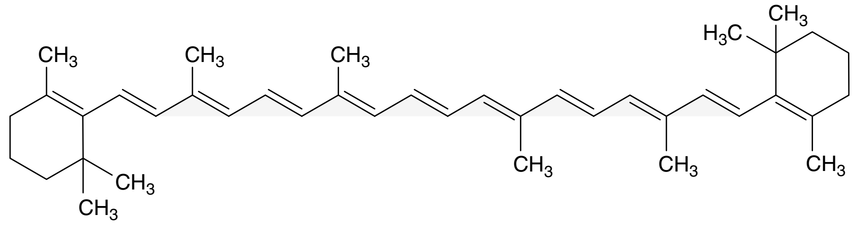
As seen from Scheme 1.19, the cation-radicals transform into radicals that are more or less stable and can be protonated reversibly. If the radicals formed are unstable, they perish before protonation. If the "initial" cation-radicals have no hydrogen atoms, their stability appears to be higher. Deprotonation is typical for cation-radicals that contain proton-active hydrogen atoms and form, after deprotonation, either quite stable or, the reverse, quite unstable radicals.

Formation of radicals having a lower energy than that of the starting cation-radicals is obviously favorable for their deprotonation. The cation-radicals of toluene and other alkylbenzenes are illustrative examples. As shown by Sehested and Holcman (1978), acidity of the medium does not prevent deprotonation of these cation-radicals.

In acetonitrile (AN), the toluene cation-radical has high thermodynamic acidity, its pK_a is between −9 and −13 (Nicholas and Arnold 1982). In the same solvent (AN), neutral toluene has



SCHEME 1.19



SCHEME 1.20

a pK_a value of +45 (Breslow and Grant 1977). One-electron oxidation of toluene causes the acidity growth by 60 pK_a units! One-electron oxidation of toluene results in the formation of a cation-radical in which the donor effect of the methyl group stabilizes the unit positive charge. Furthermore, the proton abstraction from this stabilized cation-radical leads to the conjugate base, namely, the benzyl radical. This radical also belongs to the π type. Hence, there is resonance stabilization in the benzyl radical. The stabilization is greater in the benzyl radical than in the π cation-radical of toluene. As a result, the proton expulsion appears to be a favorable reaction, and the acid–base equilibrium is shifted to the right. It is the main cause of the acidylation effects that the one-electron oxidation brings.

Unexpectedly, the pK_a value becomes less negative (acidity decreases) when electron-donating substituents are introduced in the toluene ring. Thus, the cation-radical of 4-methoxytoluene is still a strong acid, but weaker than the cation-radical of toluene itself. Baciocchi et al. (2006a) listed the following magnitudes of pK_a in AN calculated via thermodynamic cycles: −4.13 for $(4\text{—}CH_3OC_6H_4CH_3)^{+\bullet}$ and −13.5 for $(C_6H_5CH_3)^{+\bullet}$.

An interesting situation appears in the case of β-carotene (Scheme 1.20). (The cation-radical of this compound and the radical formed after its deprotonation play an important role in photosynthesis.) The question is what a methyl group will be deprotonated in this deca(methyl)cation-radical.

Gao et al. (2006) considered the data on an electron double resonance spectra of the cation-radical in conjunction with the results of calculation within the DFT. The authors established that the methyl group at the double bond of the cyclohexene ring is responsible for deprotonation of the β-carotene cation-radical. This route of proton elimination produces the most stable radical leaving the π-conjugation system to be intact. Deprotonation at the polyene methyl groups would

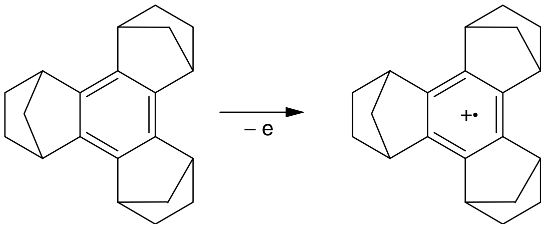
cause distortion of the π-conjugation chain and the spin would be distributed only in a part of the conjugated system.

Notably, stabilization of the cation-radical center prevents a proton from being expelled. The cation-radical of tris(bicyclopentyl)annelated benzene is not prone to proton loss, entirely, owing to the spin-charge location "more or less in the aromatic (nodal) phase" (Rathore et al. 1998b; Scheme 1.21).

In a polar solvent, heterolytic cleavage leading to proton abstraction is usually facilitated because of the favorable solvation energy of the proton, and cation-radicals are ordinarily much more acidic than the corresponding neutral compounds. Thus, the cation-radicals of 4-vinylphenols (coniferyl alcohol and isoeugenol) in a dry polar solvent are short-living species, with deprotonation to the corresponding 4-vinylpenoxyl radical being the major reaction pathway. In an acidic aqueous solution, their lifetimes are dramatically enhanced (Schepp and Rodriguez-Evora 2003). This means that in physiological conditions, these cation-radicals should be sufficiently long-lived to participate in an additional reaction with their uncharged counterparts leading to lignanlike dimers and, further, lignin. It is generally accepted that initial oxidation induced by an enzyme (e.g., peroxidase and laccase) to give (supposedly via the cation-radical) the resonance-stabilized 4-vinylphenoxyl radical is a key step. Enzyme-mediated dimerization of these 4-vinylphenoxyl radicals then leads to the production of the lignan-type materials (Davin et al. 1997). Many of the lignan-type substances have important medicinal properties (Kato et al. 1998).

Table 1.5 represents acidity constants of organic compounds (AH) and their cation-radicals ($AH^{+\bullet}$) calculated for their solutions in DMSO (a very polar solvent) at 25°C.

The acidity of the phenol-family cation-radicals depends on the stability of the corresponding phenoxyl radical, which is formed after the following proton abstraction: $(ArOH)^{+\bullet} \rightarrow H^+ + ArO^\bullet$. For instance, the radical of α-tocopherol (the radical of vitamin E) is immediately protonated to form the α-tocopherol cation-radical. The high stability of this cation-radical in mild acidic conditions is unusual when compared with many other phenols, which readily deprotonate even in strong acidic conditions (see a review by Webster 2007).



SCHEME 1.21

TABLE 1.5
Differences in pK_a Values between Aromatic Compounds and Their Cation-Radicals

AH	pK_a(AH)	pK_a($AH^{+\bullet}$)	ΔpK_a
Toluene	43.0	−20.0	63.0
Fluorene	22.6	−17.0	39.6
Phenylacetonitrile	21.9	−32.0	53.9
Phenol	18.0	−8.1	26.1
Thiophenol	10.3	−12.0	22.3

Source: Bordwell, F.G. and Cheng, J.-P., J. *Am. Chem. Soc.* 111, 1792, 1989.

For aminophenols, one-electron oxidation and the proton elimination can run together in one stage. This leads to a cation-radical containing $O^{\bullet}$ and $^{+}NH_3$ fragments within one and the same molecular carcass (Rhile et al. 2006). Such concerted reactions are classified as "proton-coupled electron transfer" (Mayer 2004). Proton-coupled electron transfer differs from conventional one-electron redox reaction in the sense that proton motion affects electron transfer. Because the transfers of a proton and an electron proceed in a single step, we can say about the hydrogen-atom transference, $(H^+ + e) \equiv H$. It is the fundamental feature of proton-coupled electron-transfer reactions that the proton and electron are transferred simultaneously, but from different places (see Tanko 2006).

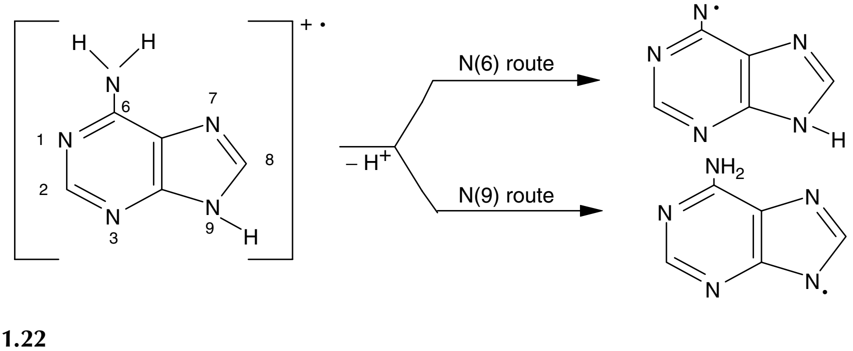
Returning to the phenol cation-radical, it is to be noted that in aqueous solutions it is characterized with a pK_a value of -2 (Dixon and Murphy 1978, Holton and Murphy 1979). Surprisingly, the pK_a value of the 2,4,6-triphenylphenol cation-radical is equal to -5 only (Land et al. 1961, Land and Porter 1963). A natural question arises: Why does the stabilization of the phenoxyl radical with the shielding phenyl groups result in such a small acidity increase? One can assume that the space shielding with the phenyl groups not only stabilizes this phenoxyl radical, but, to some extent, also hinders the proton removal. The leaving hydroxylic proton experiences not only steric hindrance, but also stoppage from complexation by the π system(s) of the phenyl ring(s).

Although the size of the leaving proton is not significant, steric hindrance for deprotonation can be appreciable. Additional examples are presented. The cumene cation-radical prefers to lose a proton from β carbon instead of α carbon. The reason for this is ascribed to the stereoelectronic effect (Zhao et al. 1999). In acid medium, either 1-anisylethanol or 1-anysyl-2-methyl-1-propanol cation-radicals undergoes C_α-H deprotonation. The deprotonation rate constant of the former is larger than that of the latter. The difference was explained by a stereoelectronic effect (Bietti et al. 2006). In general, the bulkier the α-alkyl group, the more energetically costly it is to reach the conformation most suitable for deprotonation.

Solvation of the separating proton also plays a role in regioselectivity of the cation-radical deprotonation. In this sense, steric factors are, of course, also important. Thus, the *p*-isopropyl toluene cation-radical can, in principle, expel a proton from the methyl group or from the methyne group of the $(CH_3)_2CH$ substituent. When the reaction proceeds in aqueous acetic acid, just the methyl group, being more accessible to solvation, appears to be the proton donor. The isopropyl group keeps its integrity under these conditions (Krasnikov et al. 2006).

Let us now compare the pK_a values (in AN) of the cation-radicals derived from aniline, *N*-methylaniline, and *N*-phenylaniline: 5.5, 4.2, and 1.8, respectively (Jonsson et al. 1996). An *N*-methyl substituent produces only a marginal effect on the pK_a value of the aniline cation-radical. At the same time, the effect of the *N*-phenyl substituent in aniline is considerable. The phenyl group (electron-withdrawing) effect on the aniline cation-radical acidylation is self-obvious.

Deprotonation of the adenine and guanine cation-radicals is a convenient starting position for discussing a control of this reaction from the point of relative stability of a radical formed. The proton loss is possible from the amino group at position 6 and from N(9)–H bond according to Scheme 1.22.



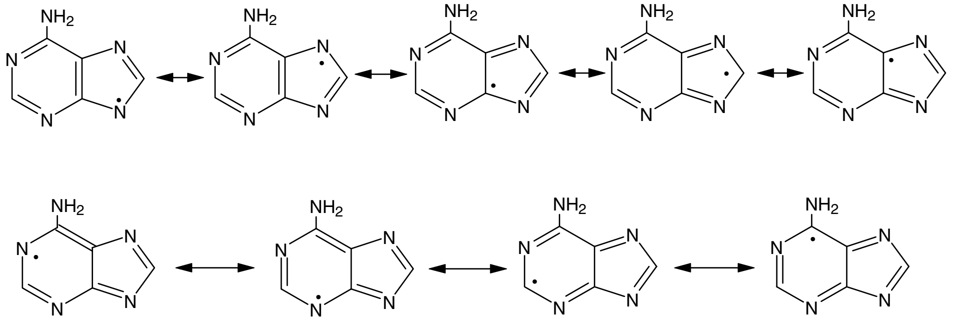
SCHEME 1.22

It is obvious that one-electron oxidation has to proceed at the expense of the lone electron pair at the group NH_2. Consequently, the 6-NH_2 deprotonation is expected. Nevertheless, the real process occurs at the expense of both 6-NH_2 and N(9)–H bond (Dias and Vieira 1996). In the N(9)-deprotonated radical, the unpaired electron is delocalized over the purine system, incorporating four nitrogen and five carbon atoms (see Scheme 1.23).

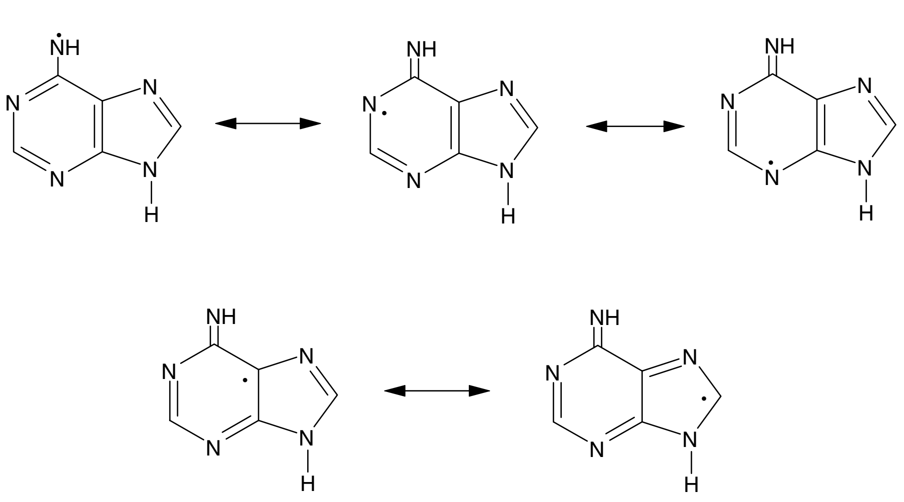
In the 6-NH_2 deprotonated radical, an unpaired electron can be delocalized over only three nitrogen atoms. These are single nitrogen of the group $NH^•$ and two nitrogens of the six-membered ring. An unpaired electron can also be delocalized over two carbon atoms (one by one of the six- and five-membered rings). This part of delocalization is depicted in Scheme 1.24.

Therefore, the N(9) radical should be more stable than the N(6) one. That is why both radicals coexist in the system and both N(9) and N(6) deprotonations take place. In the case of the guanine cation-radical, the presence of the carbonyl group in the pyridazine ring brings about two additional effects: Deprotonation infringes on this ring exclusively, and double deprotonation leads to the formation of a distonic anion-radical. Scheme 1.25 depicts the differences mentioned. Adhikary et al. (2006) substantiated it experimentally (ESR and UV) and theoretically (B3LYP).

By and large, we have a strong delocalization of the radical nonsaturation within a molecular carcass. This facilitates deprotonation of the initial cation-radicals. The same phenomenon was observed in the anion-radicals of cyclic deputies—glycine anhydride, alanine anhydride, and sarcosine anhydride (Tarabek et al. 2007).



SCHEME 1.23



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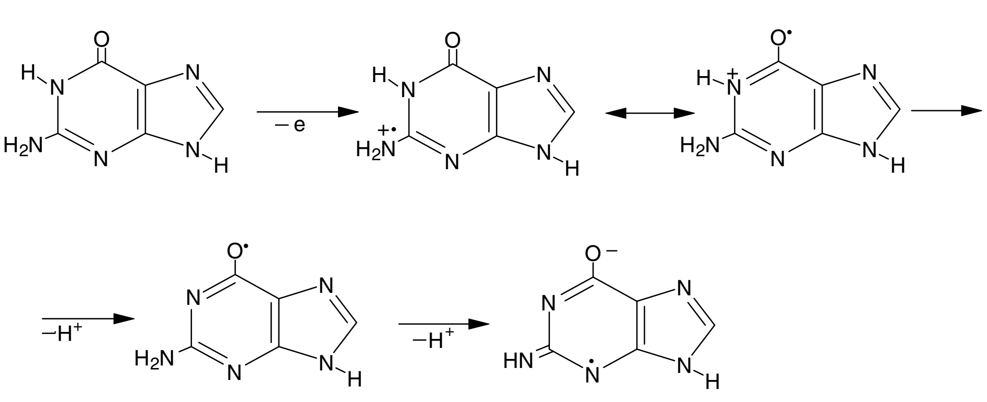


SCHEME 1.25

A potential problem when discussing the pK_a of alkylamine cation-radicals is that the deprotonation can occur on both the nitrogen and α carbon, for example,

$$(Et_2NH)^{+\bullet} \rightarrow H^+ + Et_2N^\bullet \quad \text{or} \quad (Et_2NH)^{+\bullet} \rightarrow H^+ + EtNHCH^\bullet Me$$

According to experiments (Jonsson et al. 1996), the deprotonation of $(Et_2NH)^{+\bullet}$ takes place at the nitrogen rather than at the α-carbon. However, Costentin and Saveant (2004) showed that if a stabilized carboradical can be produced, some intramolecular reorganization takes place and a proton leaves the carbon, not the nitrogen. The formation of the amine-substituted allyl radical is just the case: $^{\bullet +}NH_2\text{–}CH_2\text{=}CH\text{–}CH_2H \rightarrow H^+ + NH_2CH_2\text{=}CH\text{–}CH_2^\bullet$.

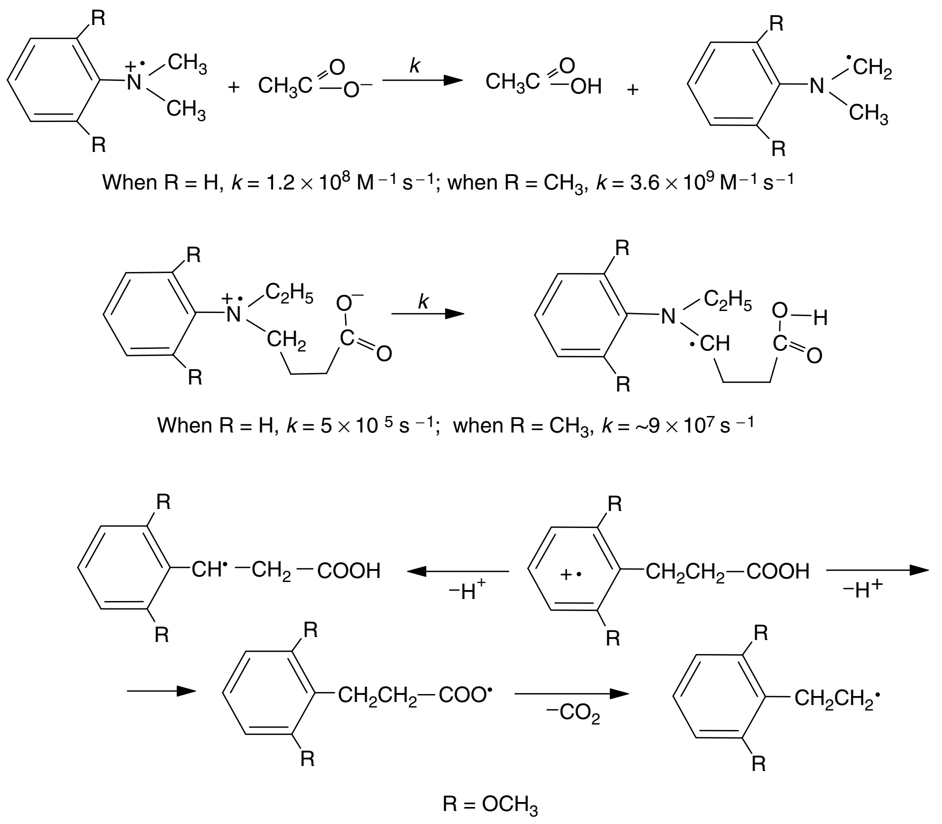
Deprotonation with the generation of the radical counterpart can be favorable as it is manifested by the low pK_a value. The dimethyl sulfide cation-radical in water is deprotonated in the following way: $[(CH_3)_2S]^{+\bullet} \rightarrow CH_3SCH_2^\bullet + H^+$. Accordingly, p$K_a$ value of $[(CH_3)_2S]^{+\bullet}$ is 0.3 from B3LYP calculations and about −1.8 from experiments (Brunelle and Rauk 2004).

All cation-radicals can be categorized as H acids on the basis of the nature of their conjugate radicals. The benzene cation-radical can be named as a σ acid because it gives the corresponding σ radical as a result of deprotonation. The toluene cation-radical gives a benzyl radical of the π type. Therefore, this cation-radical is a π acid. The phenol cation-radical should be named as a hetero-π-acid (not a hetero-σ-acid) because an unpaired electron in its conjugate base—the phenoxyl radical—is delocalized within the aromatic π system. Some amines can give cation-radicals that transform into radicals having three electrons in the field of two nuclei: $(R^1)_2N^{(+\bullet)}\text{–}CH_2R^2 \rightarrow H^+ + (R^1)_2N^{(+\bullet)}\text{–}CH^{(-)}R^2$. As a result of combining one electron from $(R^1)_2N^{(+\bullet)}$ and two electrons from $CH^{(-)}R^2$, the system acquires an additional N–C bonding and transforms into an original radical having three electrons in the field of the azomethine fragment

$$(R^1)_2N^{(+\bullet)}\text{–}CH^{(-)}R^2 \leftrightarrow (R^1)_2N^\bullet\text{=}CHR^2$$

Because the three-electron-bonded radicals are formed at the cost of the removal of the nitrogen *p*-electron, such cation-radicals should be considered as *p*-acids. Of course, the formation and behavior of these *p*-acids have to be dependent on steric factors. Works by Tomilin et al. (1996, 2000), Bietti et al. (1998), Dombrowski et al. (2005), and Yu et al. (2007) should be mentioned as describing stereoelectronic requirements to formations and configurational equilibria of *N*-alkyl-substituted cation-radicals.

Scheme 1.26 gives an indication of such a stereoelectronic effect. Using strictly comparable conditions, especially keeping medium polarity constant, Dombrowski et al. (2005) have juxtaposed



SCHEME 1.26

rate constants of proton transfer from the *N*,*N*-dialkylaniline cation-radicals to carboxylates in bimolecular reactions (see the first reaction in Scheme 1.26). As seen, the cation-radicals, in which the two *o*-methyl groups twist the $N^{+\bullet}$ center out of conjugation with the benzene ring, appear to be stronger *p*-acids. Obviously, this twist results in localization of the spin- and positive charge close to the nitrogen, preventing them from flowing out to the benzene ring. The same situation was observed in intramolecular deprotonation of a cation-radical of aniline *N*-alkylcarboxylate (see the second reaction in Scheme 1.26). The third reaction in Scheme 1.26 (the case of 3,4-dimethoxyphenylpropanoic acid) represents the competition between decarboxylation and benzylic C—H deprotonation in aqueous solutions with pH above 11 (Bieti and Capone 2006).

Now the importance of cation-radical deprotonation in oil-refining processes needs to be mentioned. Many authors note that adsorption of alkenes and alkyl aromatics on the alumosilicate surfaces leads to a marked increase in their proton acidity (e.g., Farne et al. 1972). The surface radical centers step forward as one-electron oxidants that transforms hydrocarbons in their cation-radicals: $\equiv SiO^{\bullet} + ArCH_2R \rightarrow \equiv SiO^{-} + (ArCH_2R)^{+\bullet}$. Formation of cation-radicals and their further deprotonation explain many features of the hydrocarbon catalytic transformations. Vishnetskaya and Romanovskii (1993, 1994) described the cation-radical approach of such catalytic reactions in their reviews. Generally, the formation of cation-radicals in the porous media allows obtaining the most correct data on their reactivity. For example, organic cation-radicals are usually very sensitive to surrounding nucleophilic reagents. This leads to their consumption before the deprotonation. In channels of a redox-active catalyst (e.g., in zeolites), the cation-radical deprotonation is not aggravated because competing reactions with outside reagents are precluded (Roth et al. 1997, Corma and Garcia 1998).

Concerning catalytic transformation of aliphatic hydrocarbons, an important problem is what positions are active in the deprotonation. In other words, what is the radical generated by proton abstraction from the initial cation-radical? The ESR spectra of alkane cation-radicals show that the dominant HFC is caused by hydrogen atoms of terminal methyl groups that lie in the plane of the carbon skeleton in its extended conformation. The proton loss from the cation-radical is thought to involve the C—H bond with the highest unpaired electron density (Toriyama et al. 1982). Calculations show that spin enrichment of the C—H bond leads to its elongation. This results in weakening of the C—H binding and facilitates the bond disruption (Shchapin and Chuvylkin 1996). For instance, the completely expanded cation-radical of *n*-heptane forwards its proton to the neutral parent molecule: $RH^{+\bullet} + RH \rightarrow R^{\bullet} + RH_2^{+}$.

This reaction leads to selective formation of the 1-heptyl radical (Demeyer et al. 1993). In the case of *trans*-octene-2, the cation-radical deprotonation predominantly leads to the allyl radical formation (Fel'dman et al. 1993, 1996).

$$[CH_3CH{=}CH{-}(CH_2)_4{-}CH_3]^{+\bullet} \rightarrow H^+ + (CH_2{-}CH{-}CH)^{\bullet}{-}(CH_2)_4CH_3$$

Deprotonation of alkane cation-radicals from the carbon of the highest spin density is considered as a general rule. Deprotonation of the propane cation-radical in different matrices is one principal illustration of the rule. In Freon F-113, this cation-radical expels a proton from position 2 (in the middle of the molecular carcass). In sulfur hexafluoride, deprotonation proceeds at the expense of position 1 or 3 (at the end of the cation-radical chain) (see Toriyama et al. 1982). It is clear that these different matrices stabilize different structures of the propane cation-radical. Calculations by Eriksson et al. (1994) reveal that the parent molecule has several high-lying orbitals whose energy levels are very close to one another. Potential energy surface of the propane cation-radical contains two different minima. These minima correspond to the two structures, which differ in elongation of the middle or terminal C—H bond. Details of the interaction between the propane cation-radical and a matrix define which of the minimal-energy structures appears to be more reactive.

Like any other rule, the rule of preferential deprotonation at the highest spin-density position has its exceptions. For example, in the cation-radical of silacyclohexane, the maximal spin-density atoms are carbons bonded with silicon. Nevertheless, deprotonation (in Fresno matrices) occurs preferentially from the $>SiH_2$ (Komaguchi and Shiotani 1997). The authors pointed out that the deprotonation energy from $>SiH_2$ in a silaalkane is a little smaller than that from $>CH_2$ in an alkane. This suggests that the formation of the silyl radical $>SiH^{\bullet}$ is energetically more favorable. The solvation energy and the energy of matrix arrangement can also be important factors to explain the observed high-selective deprotonation.

Recently, some attempts were undertaken to uncover the intimate mechanism of cation-radical deprotonation. Thus, the reaction of the 9-methyl-10-phenylanthracene cation-radical with 2,6-lutidine (a base) was studied (Lu et al. 2001). The reaction proceeds through two steps that involve the intermediary formation of a cation-radical/base complex before unimolecular proton transfer and separation of products. Based on the value of the kinetic isotope effect observed, it was concluded that extensive proton tunneling is involved in the proton-transfer reaction. The assumed structure of the intermediate complex involves π bonding between the unshared electron pair on nitrogen of the lutidine base with the electron-deficient π system of the cation-radical. Nonclassical cation-radicals would also be interesting reactants for such a reaction. The cation-radical of the nonclassical nature are known; see Ikeda et al. (2005) and references cited therein.

1.3.2.2 Cation-Radical Basicity

At first glance, the question of cation-radical basicity seems to be meaningless: Cation-radicals are usually strong acids. Nevertheless, these are relevant examples. Corrole and isocorrole belong to the porphyrin family and are named contracted porphyrins. They are typified by their contracted

macrocycle, one carbon less than porphyrins, but still contain four pyrrole rings (Vogel 1996). One of the pyrrole rings contains nitrogen without the N—H bond. As proven, this nitrogen accepts a proton when the free bases of corrole and isocorrole are oxidized to the cation-radicals by iodine and silver perchlorate in methylene chloride. Solutions of the protonated cation-radical remain stable for more than a week at −20°C (Endeward et al. 1998). Methylene chloride acts as a proton donor here, and the cation-radical protrudes itself as a real base. It is worth noting that methylene chloride is an extremely weak acid. Nevertheless, this cation-radical accepts a proton from such a weak proton donor. Notably, in the absence of the oxidants, the initial neutral bases are not protonated by methylene chloride!

1.3.2.3 Cation-Radicals as Acceptors or Donors of Hydrogen Atoms

Some cation-radicals can appear as hydrogen acceptors. Thus, fullerene C_{60} is oxidized to the cation-radical at a preparative scale by means of photoinduced electron transfer. As in the case of anion-radical, the fullerene C_{60} cation-radical bears the highly delocalized positive charge and shows low electrophilicity. This cation-radical reacts with various donors of atomic hydrogen (alcohols, aldehydes, and ethers) yielding the fullerene 1,2-dihydroderivatives (Siedschlag et al. 2000).

The naphthalene cation-radical can react with the hydrogen atom. The 1-hydronaphthalene cation resulting in this reaction is more stable than both the reactants. This process has no activation barrier. Being formed, the 1-hydronaphthalene cation can absorb a photon and lose one of the two hydrogen atoms on carbon 1 since these hydrogens are more weakly bound than the aromatic hydrogens. Because the C—D bond is slightly stronger than the C—H bond, the reaction mentioned here can lead to some deuterium enrichment (Bauschlicher 1998).

Reacting as H acids in solutions, a cation-radical cleaves into a radical and a solvated proton. In the gas phase, however, the homolytic cleavage typically proceeds with the generation of a hydrogen atom and an organic cation (Baciocchi et al. 2006a). Choe (2006) performed B3LYP calculations of potential energy surface and showed that the toluene cation-radical $[C_6H_5CH_3]^{+\bullet}$ can not only be the donor of a proton (with the formation of benzyl radical $C_6H_5CH_2^{\bullet}$), but also the donor of a hydrogen radical (with the formation of the energy-stabilized benzylium ion $C_6H_5CH_2^{+}$). Berberova et al. (1998) found an example of such a homolytic cleavage in solution, too. In their work, one-electron oxidation of 1,3-cyclohexadiene (C_6H_8) by 3,4-di(*tert*-butyl)-4-chloro-1,2-benzoquinone led to the formation of $C_6H_8^{+\bullet}$. In the presence of sulfur, dehydroaromatization of the following cation-radicals took place: $C_6H_8^{+\bullet} + S \rightarrow C_6H_7^{+} + HS^{\bullet}$, $2HS^{\bullet} \rightarrow HSSH$, $C_6H_7^{+} + C_6H_8 \rightarrow C_6H_7^{\bullet} + C_6H_8^{+\bullet}$, $H^{\bullet} + C_6H_6 \leftarrow C_6H_7^{\bullet} \rightarrow C_6H_6 + C_6H_8$, etc.

1.4 METALLOCOMPLEX ION-RADICALS

1.4.1 Metallocomplex Anion-Radicals

Organic anion-radicals are odd-electron species. When this odd-electron nature is retained after coordination with a metal or it emerges as a result of some redox transformation of an initial metallocomplex, the newly formed species may be unstable. As with the metallocomplex anion-radical assembling, high basicity and consequently high nucleophilicity of starting anion-radical ligands may play the decisive role in coordination with electrophilic metal-containing reactants. In other words, the electrostatic stabilization of the forming metallocomplex may compensate for these non-favoring factors. Besides, relocation of an unpaired electron from the anion-radical ligand to the central metal atom may also lead to stabilization of such complexes (see also Section 2.2.1).

For instance, the (pentaphenylcyclopentadienyl) cobalt dicarbonyl anion-radical complex $[(\eta\text{-}C_5Ph_5)Co(CO)_2]^{-\bullet}$ has $(n + 1)\,p_y$ metal orbital populated with an unpaired electron, according to calculations by Connelly et al. (1986). In contrast, reduction of $(bpy)Cr(CO)_4$ (bpy = 2,2′-bipyridyl) to its anion radical is known to occur without any major change in its structure or composition.

The ESR spectrum of $[(bpy)Cr(CO)_4]^{-\bullet}$ ion-radical resembles that of the uncoordinated $(bpy)^{-\bullet}$ anion-radical, indicating clearly that the unpaired electron is localized on the bpy ligand. This conclusion is completely corroborated by the similarity between the electronic spectra of $[(bpy)Cr(CO)_4]^{-\bullet}$ and $(bpy)^{-\bullet}$ (Vlcek et al. 1998, and references therein). Obviously, the product of one-electron reduction of $(bpy)Cr(CO)_4$ may best be formulated as a formally Cr(0) complex with an anion-radical ligand, $(bpy)^{-\bullet}Cr(CO)_4$.

There are anion-radical metallocomplexes with complete spin-retention at the anion-radical ligand (Glockle et al. 2001) as well as those having an unpaired electron on a metal atom entirely, or those that share an unpaired electron with all parts of the complex (Kaim 1987, and references therein). It is clear that the type of spin distribution depends on the participation of fragment orbitals in such an MO, which is available to be populated with the incoming electron. In terms of electron transfer, organometallic chemistry distinguishes the electron-transfer pathway (if the lowest unoccupied orbital is populated) or the hole-transfer pathway (if the highest occupied orbital is fitted with an outgoing electron). For examples, see Andersson et al. (2000).

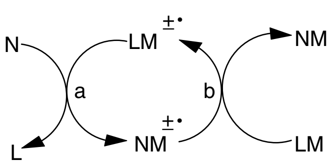
The lower the MO energy, the more probable the spin-density localization is in the framework of this MO. At the same time, coordination with a metal often decreases the energy level of the organic-ligand MO. This increases the stability of the ligand in the anion-radical form. For example, 2,1,3-thiadiazole gives an unstable anion-radical on one-electron reduction. However, this stability sharply increases if the anion-radical is coordinated with two $W(CO)_5$ fragments (at two nitrogen atoms of the thiadiazole ring) (Bock et al. 1988). If the 2,1,3-thiadiazole ring is condensed with the benzene ring, the anion-radical stability increases even without the metal coordination (Todres et al. 1969). Meanwhile, complexation with two $M(CO)_5$ fragments (M=Cr, Mo, or W) changes the ESR spectra of these anion-radicals. This means that the metal participates in spin delocalization (Bock et al. 1988).

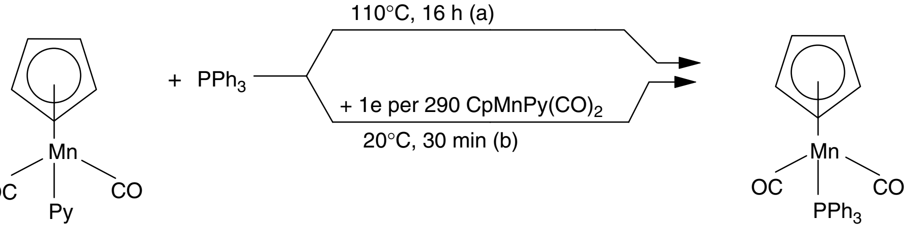
The central metal atom in complexes usually has a shell of the nearest noble gas, for example, the shell of 18 electrons. On one-electron transfer, the electron number turns from an even into an odd one (e.g., 19 for anion-radicals and 17 for cation-radicals). The one-unit change of the electron amount leads to an increase in the complex reactivity. The ligand-substitution reactions are very markedly facilitated. There are a lot of such anion-radical substitution reactions (e.g., Miholova and Vlcek 1985, Frantz et al. 2002, Panda et al. 2004, Sengupta and Panda 2005). In particular, activation of an M—CO bond for nucleophilic substitution in anion-radical metallocomplexes appears to be quite a general effect (Kaim 1987, Mao et al. 1989, 1992, Shut et al. 1995, Klein et al. 1996, Rieger and Rieger 2004). Such activation seems to be the basis of metal-cluster catalytic activity. The iron–sulfur cluster $(Bu_4N)_2Fe_4S_4(SPh)_4$ deserves to be mentioned here. The cluster is considered as a ferredoxin model (Inoue and Nagata 1986); it catalyzes an electron transfer from *n*-butyl lithium or phenyl lithium to *S*-phenyl thiobenzoate or phenylbenzoate (Inoue and Nagata 1986).

Sometimes, in ligand-substitution reactions, catalytic cycles become available. Scheme 1.27 illustrates such a cycle (Kochi 1986).

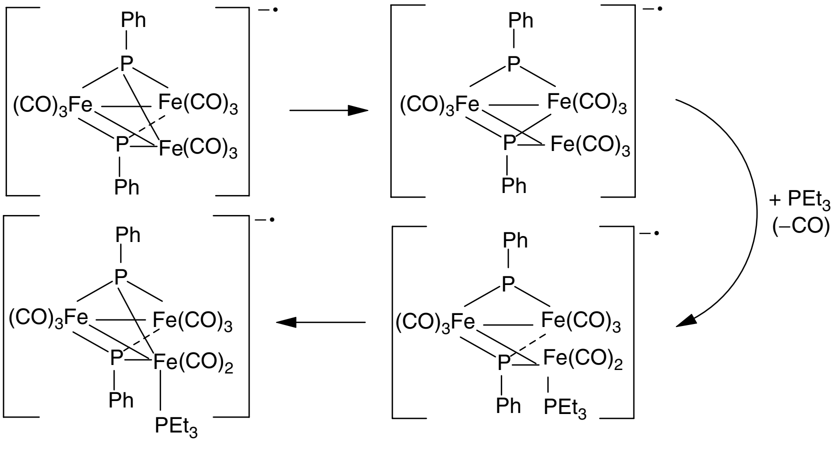
One-electron reduction of the complex starts the reaction cycle in Scheme 1.27. The anion-radical formed ($LM^{-\bullet}$) reacts with a nucleophile (N) undergoing the substitution of N for L. In doing so, the complex does not lose the unpaired electron; L-ligand is displaced out of the coordination-sphere limits. The anion-radical product $NM^{-\bullet}$ passes its unpaired electron to the initial uncharged complex LM. This results in the regeneration of the $LM^{-\bullet}$ anion-radical. The neutral product NM goes out of the catalytic cycle. Scheme 1.27 illustrates the substitution of triphenylphosphine for pyridine as a ligand in the manganese cyclopentadienyl carbonyl complex. The reaction is initiated electrochemically and only one-electron consumption is sufficient to involve 290 molecules of the initial LM complex in this transformation. The reaction completes after half an hour at room temperature. With no electron initiation, prolonged boiling in toluene is required (Kochi 1986).

Ohst and Kochi (1986) traced changes in the electron structure that takes place during the substitution of the triethyl phosphine ligand for the carbonyl ligand in the iron–phenylphosphine–carbonyl complex (see Scheme 1.28).





SCHEME 1.27



SCHEME 1.28

The initial anion-radical of Scheme 1.28 is formed from the diamagnetic ternary nuclear complex on one-electron reduction. This anion-radical undergoes spontaneous breaking of one of the phosphine–iron bond. Further substitution restores Fe–P bond, which has been opened before. Such restoration makes the whole reaction to be macroscopically reversible (in the sense of the cluster-skeleton preservation). The reaction depicted in Scheme 1.28 consists of splitting of the bridge bond between the metal and the ligand (not the metal–metal bond). It is important because this type of splitting leads to the formation of the odd-electron shell around one of the iron atoms. The iron with the odd-electron shell acquires enhanced reactivity and changes one of its ligands. Without one-electron transfer (in diamagnetic clusters), this transformation does not take place at all.

Sometimes, the ligand substitution in metallocomplexes can also proceed without reduction. The complex $Co(CO)_3L_2$ (L_2 = bis(diphenylphosphino)maleic anhydride) readily exchanges one of the carbonyl group to trialkylphosphine. Kinetic studies showed that the substitution goes through the Co–CO bond disruption. The initial complex has the tetragonal–pyramidal geometry and possesses one unfilled vacancy to coordinate an additional ligand. Studies of the complex $Co(^{13}CO)_3L_2$ by the ESR method revealed that the excess electron populates presumably the antibonding orbital of the Co–CO fragment. This bond is just weakening. The equation $Co(CO)_3L_2 + PPh_3 \rightarrow CO + Co(CO)_2L_2PPh_3$ reproduces the main point of the transformation. The initial 19-electron complex was classified as the 18-electron complex with the anion-radical ligand (Mao et al. 1989).

One-electron reduction of metalloorganic complexes or coordination between a metal and an anion-radical ligand may expand an electron shell of the central metal atom. Sometimes, anion-radical metallocomplexes contrast in this regard with the cation-radical ones. Thus, the same metalloporphyrins form cation-radicals with charges and unpaired electrons on ligands (Shinomura et al. 1981) and anion-radicals with charges and unpaired electrons on metals (Lexa et al. 1989).

Ou et al. (2004) found a way to change such a manner of the unpaired electron localization in the metalloporphyrin anion-radicals. They introduced a nitro group at only one of the eight β-pyrrolic positions of the porphyrin neutral molecule. One-electron reduction of the corresponding metalloporphyrin led to the complex with the porphyrin π anion-radical as a ligand. The nitro group is a strong electron-withdrawing group and its presence obviously lowers the energy level of the ligand-fragmental orbital of the nitro-substituted metallocomplex.

Analogously, osmium cluster with the coordinated quinoxaline was designed. The complexes are distinguished by the HOMO based on the metal and by the LUMO based strictly on the ligand. Naturally, such a complex gives rise to the anion-radical in which an unpaired electron spends all its time within the quinoxaline ligand (Nervi et al. 2003, Mottalib et al. 2005). For some reasons, the 1,10-phenathroline or benzoquinoline osmium clusters are distinguished by LUMOs that involve significant contributions from both the heterocyclic ligands and the metal atoms. One-electron reduction of these clusters leads to the anion-radicals with delocalization of an unpaired electron between both ligands and metals (Nervi et al. 2003).

At this point, 1,10-phenanthroline as a ligand should be mentioned. This ligand possesses two low-lying π* orbitals that are comparable in their energies and each is capable of accepting an excess electron. Accordingly, metal–phenanthroline complexes are easily reduced into forms containing anion-radical phenanthroline ligands (Mirochnik et al. 2003).

1.4.2 Metallocomplex Cation-Radicals

There is a large volume of literature describing one-electron oxidation of metallocomplexes. Such abundance is caused by the chemical nature of metallocomplexes in which the metallic center readily transforms into a higher state of oxidation. Kochi (1986) and Kaim (1987) have covered many of these problems in their reviews. Astruc (1995) has done a very important generalization in the field.

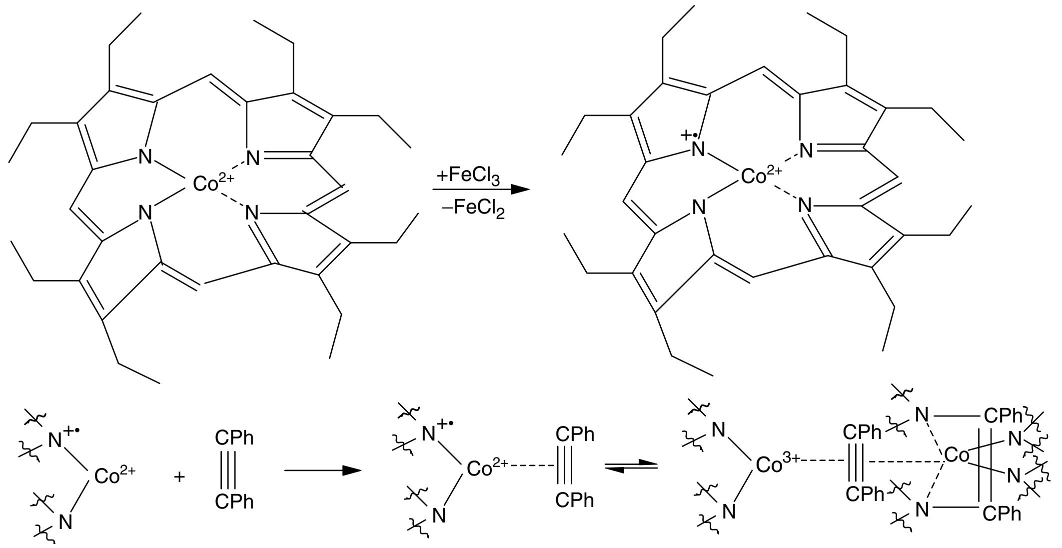
One of the most important intricacies in the redox chemistry of organyl metallocomplexes is that both a metal and a ligand can be involved in oxidation. The following examples illustrate both the possibilities and manifest the corresponding consequences in chemical reactivity of the complexes.

The copper–porphyrin complex gives cation-radicals significant reactivity at the molecular periphery. This reactivity appears to be that of nucleophilic attack on the cation-radical, which belongs to the π type (Ehlinger and Scheidt 1999). The cobalt–porphyrin complex gives rise to the cation-radical with charge-spin localization at the nitrogen atom of the porphyrin ring. The cation-radical thus formed acquires an enhanced reactivity and can add tolane (Kochi 1986) (Scheme 1.29).

The main point of transformation in Scheme 1.29 is that the central cobalt atom eventually becomes an electron reservoir.

Alike metallocomplex anion-radicals, cation-radicals of odd-electron structure exhibit enforced reactivity. Thus, the 17-electron cyclopentadienyl dicarbonyl cobalt cation-radical $[CoCp(CO)_2]^{+\bullet}$ undergoes an unusual organometallic chemical reaction with the neutral parent complex. The reaction leads to $[Co_2Cp_2(CO)_4]^{+\bullet}$. This dimeric cation-radical contains a metal–metal bond unsupported by bridging ligands. The Co—Co bond happens to be robust and persists in all further transformations of the binuclear cation-radical (Nafady et al. 2006).

Reversible one-electron oxidation of ferrocene (Fc) and its derivatives toward cation-radicals (the so-called ferrocenium cations) is a well-known reaction. The cation-radical center is localized at the iron atom. According to photoelectronic spectra and voltammetry data, such localization is



SCHEME 1.29

kept in ferrocenium derivatives containing electron donor substituents in conjugation with one of cyclopentadienyl rings (Todres et al. 1992a, 1992b; Novak and Kovac 2006). As a rule, one-electron oxidation of the central iron atom proceeds earlier than that of donor substituents in ferrocenes (see also Ogawa et al. 2006, Colbran et al. 2006). When *cis*-ferrocenylacrylonitrile has been converted into the cation-radical, no cis → trans isomerization is observed (Todres 1987). However, this conversion is common for homoaromatic cation-radicals of the stilbene series. The difference was explained with a marked distinction by the nature of the cation-radical under comparison. In homoaromatic cation-radicals, the MOs, which are populated by an unpaired electron, embrace all the π orbitals. For the ferrocenylacrylonitrile cation-radical, a single electron remains exclusively on the atomic orbital of iron. In this cation-radical, one of the next adjacent orbital of a higher level belongs to the acrylonitrilic fragment. If such an orbital is involved in the process of oxidation, rotation around the ethylenic bond is predicted to occur (Todres et al. 1992b). This would be important for the usage of ferrocenylethylenes in optoelectronic devices. There is evidence that the first-step oxidation of 1,2-diferrocenyl-1,2-diphenylethylene consists of one-electron removal from the second, rather than the first, HOMO (Bildstein et al. 2004). This regularity is a breakdown of Koopman's theorem such a breakdown is widespread in organometallic chemistry. In particular, such an inadequacy of ferrocenes was pointed out by Ishimura et al. (2002).

1,4-Divinylbenzene bearing two ferrocenyl substituents at the two terminal carbon atoms of the vinyl group—1,4-bis(ω-ferrocenylvinyl)benzene—represents an example important for our consideration. This compound exhibits a single wave on electrochemical oxidation. Controlled-potential coulometric test presented the consumption of two electrons per molecule. It would be possible to conclude that the system belongs to class III of the Robin and Day (1967) categorization, when the two oxidative centers are completely equivalent in the sense of spin-density localization in the half-to-half manner between both ferrocenyl substituents in the preliminary obtaining cation-radical. However, application of rapid-scan time-resolved Fourier transform infrared spectroscopy led to another conclusion. It was proven that one ferrocenyl fragment was oxidized first resulting in the formation of the partly delocalized cation-radical. Then, as the first-step oxidation continues, the other ferrocenyl fragment was also oxidized resulting in the formation of the dication

(Jin et al. 2007). In other words, an intermediate coupling between the mixed-valence centers exists. Therefore, referral of this diferrocenyl compound to the Robin–Day class II category is more appropriate.

Ratera et al. (2003) discovered valence tautomerism in the ferrocene connected through the ethylenic bond with perchlorotriphenylmethyl radical. As ascertained by Moessbauer spectroscopy, this species in the solid state exhibited a thermally induced intramolecular electron transfer resulting in the formation of ferrocenium and perchlorotriphenylmethyl anion moieties. The authors used the initial species in its trans form. If the cis form would be available, the possibility of rotation around the ethylenic bond would be interesting to disclose. According to the authors, the interconversion of the cation-radical and anion centers proceeds gradually. At ambient temperature, equilibrium composition of the tautomers is achieved. This peculiarity is important with respect to potential technical applications.

It would also be interesting to check the ability of the ruthenocene acrylonitrile cation-radical to rotate around the ethylene bond: Ruthenocenyl is weaker than ferrocenyl as a donor substituent (Laus et al. 2005). The particular property of rotating around the ethylenic bond in cation-radicals is a method of elucidating an electronic structure.

It needs to be noted that the problem of electronic tautomerism also includes thermal transformation of neutral metalloorganic compounds into cation-radical states. Two examples concerning organomolybdenum complexes can be exemplified. The first example relates to the complex containing bis-2,9-di(4-aminophenyl)-1,10-phenanthroline, $^{2-}O_{18}Mo^{VI}{}_6{=}N{-}C_6H_4PhenthC_6H_4{-}N{=}Mo^{VI}{}_6O_{18}{}^{2-}$. This complex gives a broad-line ESR spectrum at room temperature. At a low temperature (35 K), a narrow-line spectrum that contains two peaks was recorded. One peak is associated with a localized unpaired electron (cation-radical) in the 2,9-diphenylphenanthroline ligand. Another peak in the spectrum can be associated with a localized electron (Mo^V) in the hexamolybdate moiety. Integration of the ESR peaks indicated that only a fraction (5–10%) of the hexamolybdate complex was paramagnetic on the ESR time scale. Bar-Nahum et al. (2005) ascribe the facts observed to the following equilibrium between the valence tautomers:

$$^{2-}O_{18}Mo^{VI}{}_6{=}N{-}C_6H_4PhenthC_6H_4{-}N{=}Mo^{VI}{}_6O_{18}{}^{2-} \rightarrow$$

$$^{2-}O_{18}Mo^{VI}{}_6{=}N{-}[{-}C_6H_4PhenthC_6H_4{-}]^{+\bullet}{-}N{=}Mo^{VI}{}_5Mo^{V}O_{18}{}^{2-}$$

The second example refers to oxomolybdenum dithiolate complex $[Mo^VO(qdt)_2]^{1-}$, where qdt stands for quinoxaline-2,3-dithiolate. This complex also manifests thermal valence isomerism. Helton et al. (2001) also explain it with the change of the molybdenum oxidation state:

$$[(qdt)Mo^VO(qdt)]^{1-} \rightarrow [(qdt)Mo^{IV}O(qdt)^{+\bullet}]^{1-}$$

It is also worth noting metallocomplexes containing carbene cation-radicals as ligands. Carbenes are neutral molecules with a dicoordinate carbon atom having two nonbonding electrons. As a rule, carbenes are highly basic and as ligands they are strong electron donors and poor electron acceptors. This feature of carbene as ligands allows redistributing electron density within organometallic complexes: The central metallic atom picks up one electron from the carbene ligand (e.g., $Cu^{2+} \rightarrow Cu^{1+}$), whereas the ligand transforms into the carbene cation-radical ($>C^{\bullet\bullet} \rightarrow >C^{+\bullet}$). Kraft et al. (2002) have given an example of such a redistribution. At this point, it needs to be noted that the literature also represents transitions of free carbenes into carbene cation-radicals on oxidation, for example, using ferrocene as a one-electron oxidant (Ramnial et al. 2004).

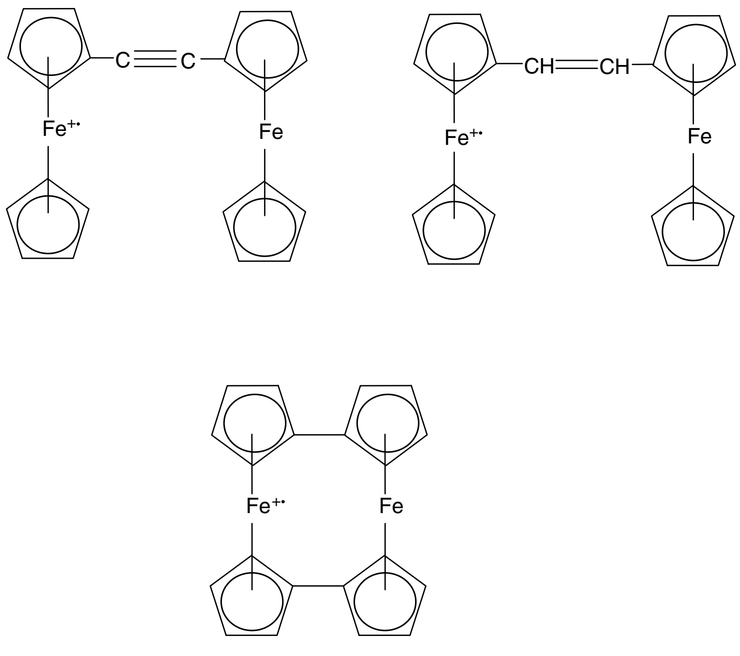
1.4.3 Bridge Effect in Metallocomplex Ion-Radicals

Technically useful properties of organometallic complexes are, in many respects, connected with the ability to give up one electron. The bridge effect can connect or separate different sites of the nonmononuclear cation-radical metallocomplexes. Changes in the nature of the bridge allow fine-tuning the signal transmission in electronic devices.

Thus, electron-spin spectroscopy clearly documents that a long-range interaction exists between the two metal centers in the cation-radical of 9,10-bis[(η^5-cyclopentadienylmethyl)(η^6-cycloheptatriene)rhodium]anthracene, which arises from the one-electron oxidation of the neutral complex. However, the odd electron is delocalized over the whole rhodium–anthrylene–rhodium system only if this bridge has optimal geometry. The optimal geometry means that the two cyclopentadienyl-RhL_2 moieties assume a *trans* conformation relative to the 9,10-anthrylene plane with both the metal centers facing the aromatic system (Carano et al. 2001, Cicogna et al. 2004).

Donor ability and the absence of steric hindrance in the bridge are favorable to the stability of the metallocomplex cation-radicals. For example, the cation-radical prepared from the complex containing two molybdenum centers connected with the $Me_2P–CH_2CH_2–PMe_2$ bridge and coordinated with the cyclopentadienyl and carbonyl ligands appears to be much more stable than the analog connected with the $Ph_2P–CH_2CH_2–PPh_2$ bridge (Alvarez et al. 2004).

The bridge effect was scrutinized in the range of diferrocenyl derivatives, especially of those that are applicable in catalysis and material science (Atkinson et al. 2004). One-electron oxidation of these derivatives also proceeds easily, reversibly, and gives rise to cation-radicals (ferrocenium ions). In contrast to the cation-radical of ferrocenylacrylonitrile, the hole transfers through conjugated systems were proven for the bis(ferrocenyl)acetylene cation-radical (Masuda and Shimizu 2006), the bis(ferrocenyl) ethylene cation-radical (Delgado-Pena et al. 1983), and the cation-radical of bis(fulvaleneiron) (LeVanda et al. 1976). These structures are presented in Scheme 1.30.



SCHEME 1.30

Extended Hueckel MO calculations (Kirchner et al. 1976) support the statement that the unpaired electron is delocalized over both metallocene residues in the bis(fulvaleneiron) cation-radical (the third structure in Scheme 1.30). Alternatively, very fast intraionic intervalence electron transfer may take place between the formal Fe(II) and Fe(III) atoms of this structure. Intervalence electron transfer in such π-bridged systems may proceed either by superexchange or jumping mechanism. During superexchange, the electron (hole) is never vibronically localized on the bridge. During jumping, the electron (hole) is vibronically localized on the bridge for a short time. Within both the mechanisms, the electron (hole) transfer occurs very fast. No cis → trans isomerization was reported for the cation-radical of 1,2-diferrocenylethylene (the second structure of Scheme 1.30). Obviously, the exocyclic double bond has no time to rotate during intervalence electron transfer in $[Fc–CH=CH–Fc]^{+\bullet}$ cation-radical.

Lloveras et al. (2005) compared intervalence electron transfer in 1,4-diferrocenyl-1,3-butadiene, $[Fc–CH=CH–CH=CH–Fc]^{+\bullet}$ and in 1,4-diferrocenyl-2-aza-1,3-butadiene, $[Fc–CH=N–CH=CH–Fc]^{+\bullet}$. Although intervalence electron transfer in $[Fc–CH=CH–CH=CH–Fc]^{+\bullet}$ and $[Fc–CH=CH–Fc]^{+\bullet}$ resemble each other, this process in $[Fc–CH=N–CH=CH–Fc]^{+\bullet}$ is restricted to some degree. As the authors noted, "the population of the state with the positive charge located on the iron attached to the 4-position of the 2-aza-1,3-butadiene bridge is dominant, with just a very small population (<0.1%) of the state with the charge on the other iron site" (Lloveras et al. 2005).

Significant electronic interaction between the iron centers was also found in the cation-radicals of diferrocenylthiazoles (Tarraga et al. 2002, Plazuk et al. 2005) and in the cation-radical of Fc(Ph)C=C=C=C=C=C(Ph)Fc cumulene molecular wire (Skibar et al. 2004). In the latter cation-radical, an unpaired electron (a hole) is half-to-half localized on each Fe atom. "No apparent spin density was found on the cumulene chain" (Bildstein et al. 2004).

When several ferrocenyl substituents have one and the same conjugating bridge, they are oxidized into the corresponding ferrocenium derivatives in a stepwise way (class III categorization by Robin and Day [1967]). In particular, volt–ampere curves have several one-electron reversible waves, the amount of which is equal to the amount of the ferrocenyl substituents. If conjugation between these substituents is absent (Robin–Day's class I), oxidation is concerted, and one wave is observed. This wave is merged, corresponds to many electrons, and is still reversible. In this sense, 1,3,5-tris(ferrocenyl)benzene (1,3,5-$Fc_3C_6H_3$) is of interest as the trication–triradical precursor. All of the three substituents occupy meta positions with respect to one another—they are not conjugated. As could be expected, 1,3,5-$Fc_3C_6H_3$ should give one three-electron reversible anodic wave during anodic oxidation. Nevertheless, its electrochemical oxidation occurs in two distinct steps involving one and two electrons and proceeds reversibly (Li et al. 2006). It is structural peculiarities that cause such a special behavior: In 1,3,5-$Fc_3C_6H_3$, two ferrocenyl groups are located above the benzene ring. These two substituents are equivalent and brought together. The third ferrocenyl is located below the plane of the benzene ring (Stepnika et al. 1997). Using the Hueckel approach, Li et al. (2006) estimated the HOMO energy levels for 1,3,5-$Fc_3C_6H_3$, 1,3-Fc_2-5-$Fc^+C_6H_5$, 1-Fc-3,5-$(Fc^+)_2$, and 1,3,5-$(Fc^+)_3C_6H_3$. The levels are in the following and surprising sequence: −4.88 eV [1,3,5-$Fc_3C_6H_3$], −5.37 eV [1,3-Fc_2-5-$Fc^+C_6H_5$], −5.42 eV [1-Fc-3,5-$(Fc^+)_2$], and −5.42 eV [1,3,5-$(Fc^+)_3C_6H_3$]. Equality of the latter two magnitudes correlates with the electrochemical data. It is difficult to assume conjugation between the two ferrocenyl fragments that are located in meta position to each other. Their equal spatial orientation supposedly defines the equivalency in HOMO energies and oxidation potentials.

An interesting picture was revealed by Gouverd et al. (2006) as a result of comparison between the neutral chromium tricarbonyl complex of *C,P*-diaryl phosphaalkene [$(CO)_3Cr$←PhCH=PMes*] and its anion-radical {$[(CO)_3Cr \leftarrow PhCH=PMes^*]^{-\bullet}$} (Mes* is 2,4,6-tris(*tert*-butyl)phenyl). According to the ESR and DFT data for the anion-radical, about 40% of the negative charge is localized on $Cr(CO)_3$ moiety. This is understandable if one takes into account the known electron-acceptor

nature of the chromium tricarbonyl group. What is surprising is that the main part of the spin density (up to 60%) is localized at the more remote phosphorous, but not at the closer methine of (CH=P) moiety. Perhaps, the formerly vacant phosphorus orbitals (absent for the carbon) play a role in holding off the spin density in the anion-radical considered.

1.4.4 Charge-Transfer Coordination to Metallocomplex Ion-Radicals

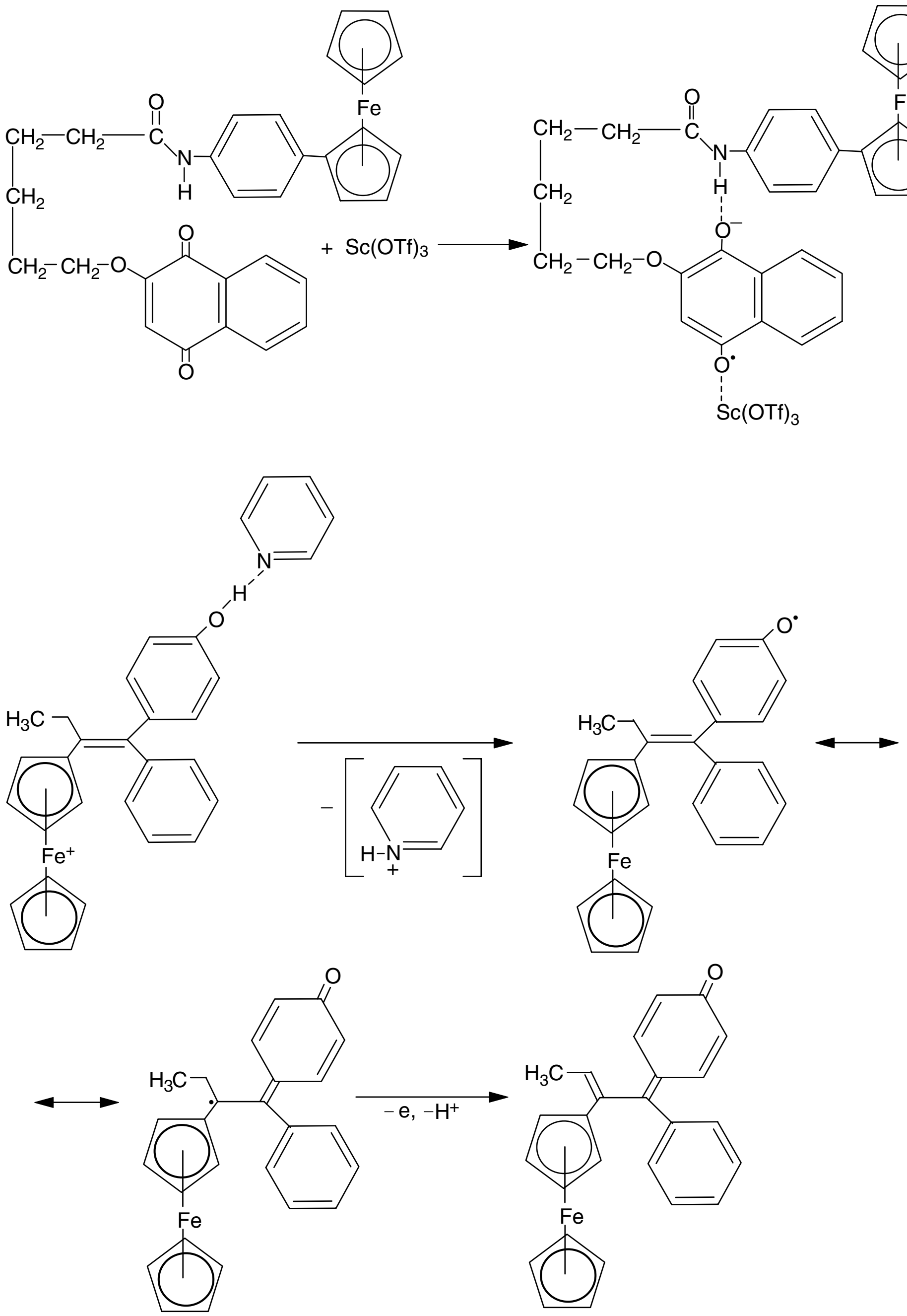
This problem will be considered on the basis of charge-transfer coordination of organic polynitriles to substituted ferrocenes. The practical significance of the charge-transfer coordinative species (salts) is their ferromagnetic behavior (see Section 8.5). The salts contain the cation-radical and anion-radical counterparts. Peculiarities in electronic structures of the cation-radical parts within the salts are topics of our interest.

Oxidation of alkyl ferrocenyl phosphines, Fc_2PAlk, with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) yields 1:1 salts (Durfey et al. 2004). The common negatively charged part of these salts is $(DDQ)^{-\bullet}$. As with the positively charged parts, their Moessbauer spectra point out that Fe^{II} state is retained. This suggests that these parts do not result in the net removal of an electron with the formation of the ferrocenium moieties, at least in the solid state. Electron-spin resonance spectra are consistent with $(DDQ)^{-\bullet}$ only. No signals for ferrocenium, phosphorus, or non-$(DDQ)^{-\bullet}$ carbon centers were observed. This prevents the final conclusion on the location of the positive charge in the ferrocenyl moiety of the cation-radicals formed. More importantly, orange-red color of the salts suggests that the iron is present as Fe^{II}. Ferrocenium ions have a characteristic green or blue-green hue. Durfey et al. 2004 presume that "oxidation occurs at phosphorus or ligand rather than at iron." From the materials mentioned earlier, it is evident that such a direction of the one-electron oxidation is unusual for the ferrocene series and can be ascribed to the presence of the phosphorus lone electron pair in the initial ferrocene derivatives.

From this point of view, it would be important to mention the result of DDQ one-electron oxidation of $Fc_2P(=O)Alk$ (Barriere et al. 2005) and $Fc_2P(=O)Ph$ (Durfey et al. 2000). The Moessbauer spectra of $[Fc_2P(=O)Et]^{+\bullet}[DDQ]^{-\bullet}$ and $[Fc_2P(=O)Ph]^{+\bullet}[DDQ]_2^{-\bullet}$ confirm the presence of two types of iron, namely, Fe^{II} and Fe^{III}. At 77 K, the Moessbauer spectra indicate that the electron transfer is incomplete. The percentage of oxidized species is less than 50, but increases with temperature. This increase may be a consequence of electron transfer inside the ion-radical salt. Higher temperature may assist in electron transfer from iron to DDQ, whereas lower temperature is favorable in the reduction of Fe^{III} at the expense of $(DDQ)^{-\bullet}$. Other explanations of the electron redistribution in these ion-radicals are also possible. This case of the bridge effect remains perplexing and deserves further experimental and theoretical study.

It should be pointed out that the treatment of phosphorus or sulfur donors bearing ferrocenyl groups with diiodine results in the formation of molecular charge-transfer adducts without simultaneous oxidation of the ferrocenyl groups (Durfey et al. 2000, Gridunova et al. 1982). At the same time, the reaction of 4-ferrocenyl-1,3-dithiolene-2-thione with diiodine leads to a charge-transfer complex in which the iron has been oxidized from Fe^{II} to Fe^{III}. This was confirmed by magnetic measurements and Moessbauer spectroscopy (Allen et al. 2003).

In contrast, ferrocene, 1,1′-dimethylferrocene, decamethylferrocene, and 1,2-diferrocenylethane all react with DDQ forming a dark green 1:1 ion-radical salt. Both $(DDQ)^{-\bullet}$ and ferrocenium constituents of the salts were characterized by their typical electron spectra (Salman et al. 2004). Sometimes, even a weak charge transfer can transform the ferrocenyl substituent into the full-value hole reservoir acting intramolecularly. Scheme 1.31 gives two such examples. One of them describes the effect of charge-transfer coordination between Sc^{3+} as an acceptor and a ferrocene derivative as a donor (Okamoto et al. 2003). The other example introduces the effect of charge-transfer coordination between pyridine as a donor and a ferrocenium derivative as an acceptor (Hillard et al. 2006).



SCHEME 1.31

1.5 ORGANIC ION-RADICALS WITH SEVERAL UNPAIRED ELECTRONS OR CHARGES

In principle, an organic molecule can accept as many electron pairs as it has low-lying vacant orbitals. In the same way, high-lying occupied orbitals can release not a single, but several electrons. Such multielectron processes can result in the formation of polyion-polyradicals. As will be seen from this section, the main topic of interest in poly(ion-radicals) consists of their spin multiplicity.

Therefore, the following consideration of the corresponding negatively and positively charged species emphasizes their electronic structures.

Anion-radicals are the first products of reductive electron transfer. Mutual repulsion of the primary and subsequent excess electrons forms the basis of the impediment of polyelectron reduction at the initial step. However, an orbital, which already has one electron, can be populated by another electron if a proper reducer is chosen. This reducer must be able to overcome Coulomb repulsion. As a result, more or less stable dianions are formed. Like anion-radicals, dianions can reversibly give excessive electrons back. If skeleton rearrangement is absent, the initial uncharged molecules are regenerated.

In dianion-diradicals, two vacant orbitals are populated, that is, LUMO and the next (somewhat higher) unoccupied one. This next orbital must, nevertheless, be situated low enough. Such an orbital can be detected in molecules of unsaturated hydrocarbons of a widespread contour. Within this expanded contour, extensible electron delocalization somewhat decreases the repulsion energy. Several electron-acceptor fragments (substituents with heteroatoms or with high conjugation ability) assist in the formation of poly(anion-radicals).

When there are two electron-acceptor fragments in the reducing molecule, the mechanism of consecutive one-electron transfers depends on the relative electron affinity of these fragments. Zheng and Evans (2003) considered the formation of dianion-diradicals from molecules bearing two reducible groups (A^1 and A^2) separated by a spacer unit (S), A^1-S-A^2. If $A^1 = A^2$ and S is short or unsaturated, it is significantly costlier in energy to insert the second electron than the first one. When $A^1 = A^2$ but S is long or, especially, saturated, the two electron-accepting group can act independently and even at the same time. If A^1 and A^2 are different, and S is long, two cases are distinguished. When A^1 is more active than A^2, two well-separated one-electron transfer takes place. When S is still long, but electron affinities of different A^1 and A^2 are close, the probability of the first electron entering at A^1 and A^2 is almost equal. In this case, A^1 can accept an electron before A^2 or A^2 can be reduced first. A two-step mechanism is also possible: One of the acceptor groups perceives an electron, transfers it to the other group (by the jumping or superexchanging manner), and then captures one electron more. The analogous approach is applicable to the formation of the corresponding dication-diradicals.

Because poly(anion-radical)s are polycharged species, they are very prone to associating with counterions. The association decreases the total energy of the system, increases its stability, and facilitates its formation. The formation of poly(anion-radical)s is usually successful, if alkali metals are used as reducers in dimethoxyethane (DME), THF, or MeTHF as solvents. Medium components, for example, hexamethyl phosphotriamide (HMPA) or cryptands, which weaken ion-pair interaction, work unfavorably. Even traces of proton admixtures evoke a transformation of reducing compounds into hydrogenated products instead of polycharged anions. As a rule, the higher the charge of a particle to be prepared, the lower must be the temperature and the longer should be the contact with a reductant. Of course, working with such species requires an inert atmosphere.

Poly(ion-radical)s are of interest today first because of their possible application in microelectronics. Therefore, spin distribution is very important for these species. New organic triplet poly(ion-radical)s, with strong intramolecular ferromagnetic coupling and good thermal stability may serve as building blocks for organic magnets. For example, sodium reduction of bis(dimesitylboron)-1, 3-phenylene in 2-methyltetrahydrofuran-tetrahydrofuran (MeTHF-THF) mixture leads to the corresponding dianion-diradical as a species of a triplet state (Rajca et al. 1995).

In the case of 1,8-diphenylnaphthalene, there is an interesting difference in the spin states of the anion-radical on one hand, and of the trianion-radical on the other. In the anion-radical, the main contour for spin distribution is the naphthalene framework. In the trianion-radical, the naphthalene π system bears two electrons (nonassociated with any bond), whereas the third (unpaired) electron oscillates between 1 and 8-phenyl substituents (Gerson and Huber 1987).

Tetracyanoquinodimethide is able to give both anion-radical and dianion. It is unable to form the trianion-radical. However, with widespread π-electron contour, the trianion-radical exists—such

a form was described for tetracyano-2,7-pyrenoquinodimethide (Gerson et al. 1983). The anion-radical of tetracyano-2,7-pyrenoquinodimethide contains "a half" electron at each dicyanomethide group (class III of the Robin–Day categorization). The corresponding dianion holds "the whole" electron at each dicyanomethide group, and the trianion-radical has one electron at each fragment $C(CN)_2$ and one (the third) electron even in the arene π system (Gerson and Huber 1987). This trianion-radical was also described as an anion-radical bearing two negatively charged dicyanomethide groups (Rieger et al. 1963).

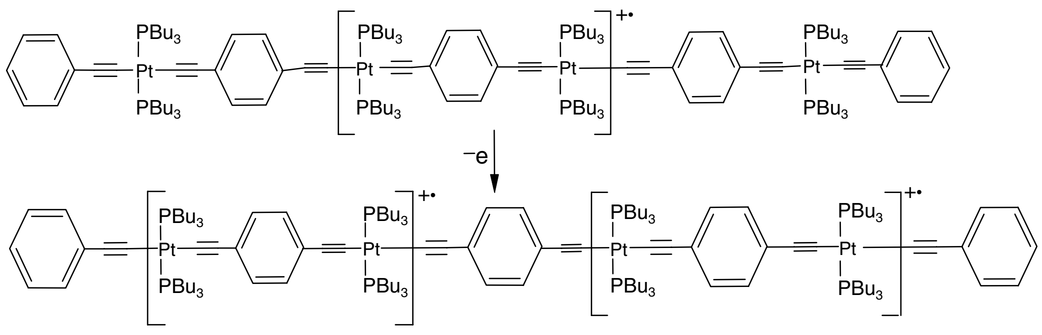
The dianion-diradical is formed on two-electron reduction of 1,2-bis(cyclooctatetraeneoxy) ethane, C_8H_7–OCH_2–CH_2O–C_8H_7. This dianion-diradical contains two almost planar rings of C_8H_7 and each of them bears one excess electron with no electron–electron coupling. No electron coupling was also observed in ($C_8H_7^{-\bullet}$)–OCH_2–CHO($C_8H_7^{-\bullet}$)–CH_2O–($C_8H_7^{-\bullet}$) trianion-triradical (Stevenson et al. 2005). The authors ascribe stability of these poly(anion-radical)s to the tube → planar changes that each cyclooctatetraene undergoes in a result of one-electron reduction. Electron–electron repulsion also assists in the stability of these poly(anion-radical)s, preventing their transformation into polydianions. In this case, such a repulsion prevails over the aspiration of the cylooctatetraene anion-radical to add the second electron and to transform into the dianion according to $2n + 2$ Hueckel rule for planar aromatic monocyclic systems.

Analogous phenomena were observed in cation-radicals of platinum acetylide oligomers; one example is represented by Scheme 1.32 (Cardolaccia et al. 2007). As it follows from electrochemical, UV-visible spectral and DFT theoretical studies, the cation-radical of Scheme 1.32 contains only one spin-charge link in the center of the species. Two-electron oxidation of the parent neutral molecule leads to localization of the two cation-radical parts over two repeated units. In other words, the two cation-radical fragments exist in relative proximity and are connected with the diacetylenyl phenylene bridge. Nevertheless, this dication-diradical is favored over the dication as a nonspin particle. According to Cardolaccia et al. (2007), stabilization of the dication-diradical electronic structure may be driven by several factors including the distortion in geometry (phenylene rotations and bond length changes) as well as the fact that π delocalization through the platinum centers is not very efficient. No magnetic properties of the dication-diradicals of this family have been published yet.

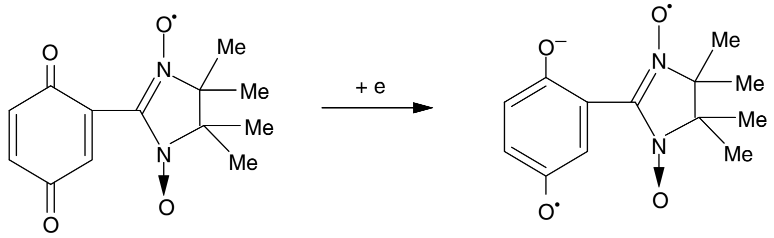
Several anion-biradicals have been recently reported, which are composed of semiquinone and nitroxide functionalities. Such anion-biradicals are obtained by electron transfer to the *p*-benzoquinone (BQ) substituted by a nitronyl (Shultz and Farmer 1998) or nitronyl-nitroxide (NN) group (Kumai et al. 1994). Scheme 1.33 gives the BQNN example.

The anion-diradical $(BQNN)^{-\bullet}$ has two nondegenerated SOMOs. One is delocalized over the entire molecule and the other (SOMO′) is localized within the NN group.

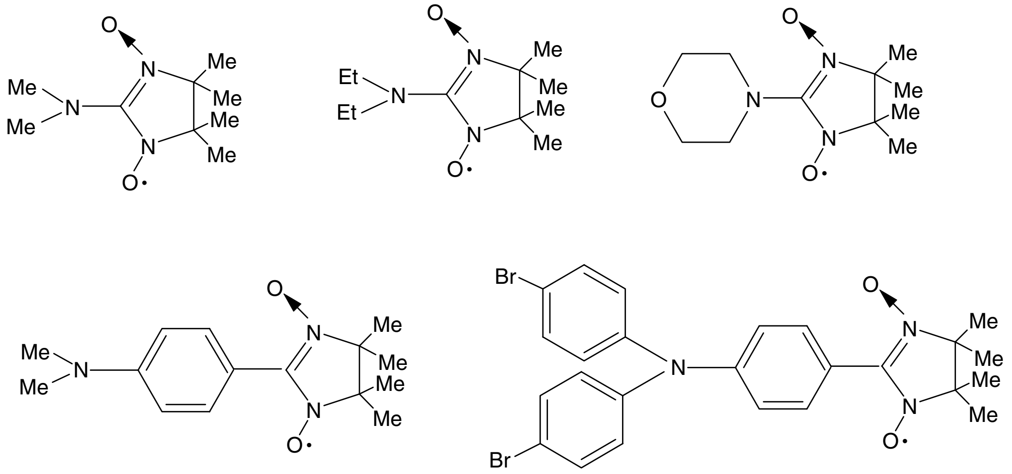
The same Japanese crew has prepared open-shell molecules carrying the NN groups (Sakurai et al. 1996, 2000; Kumai et al. 1996). These donors are presented in Scheme 1.34. The corresponding



SCHEME 1.32



SCHEME 1.33

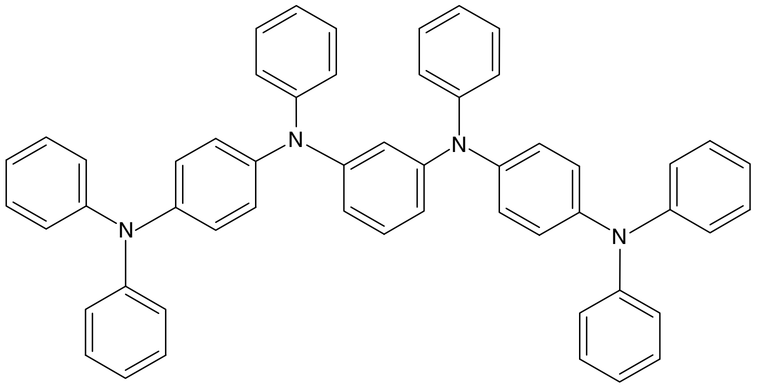


SCHEME 1.34

products of the one-electron oxidation have been designed as the cation-radical analogs to the anion-radical counterparts in Scheme 1.33.

All the mentioned donors were oxidized by excess I_2 in THF or MeTHF. ESR spectroscopy at cryogenic temperatures (6–110 K) established the paramagnetic nature of the oxidized products. To rationalize the ground-state spin multiplicity, the MO calculations were performed on these paramagnetic species. The results strongly suggested that the species exist as cation-radicals with triplet ground states. There are two nondegenerated SOMO and SOMO′; the delocalized spin on the donor site and the localized spin on the radical site in these cation-diradicals are oriented in a parallel (antiferromagnetic) manner. Even triphenylamine bearing the same NN substituent at the para position of each phenyl ring gives the cation-radical of the paramagnetic, but antiferromagnetic type. The oxidation of such symmetrically substituted triphenylamine was performed with tris(4-bromophenyl)ammoniumyl hexachloroantimonate in frozen butyronitrile at 123 K, magnetic measurements were carried out for the microcrystalline samples in the temperature range 2–300 K (Nakano et al. 2005). The observed antiparallel type of spin orientation does not lead to magnetism of organic materials.

An extensive body of published materials is devoted to the ammoniumyl derivatives bearing either alkyl or aryl groups at the nitrogen atoms. *N*,*N*-Dialkylanilines are oxidized very easily, but give rise to unstable cation-radicals. Oxidation of *N*,*N*-diarylanilines proceeds with some difficulty, but leads to more stable cation-radicals. As a useful compromise, *N*,*N*-bis(*p*-methoxyphenyl) aniline was distinguished (Kwon et al. 2005). The corresponding cation-radical is obtained as easily as that from *N*,*N*-dialkylaniline, but appears to be much more stable.



SCHEME 1.35

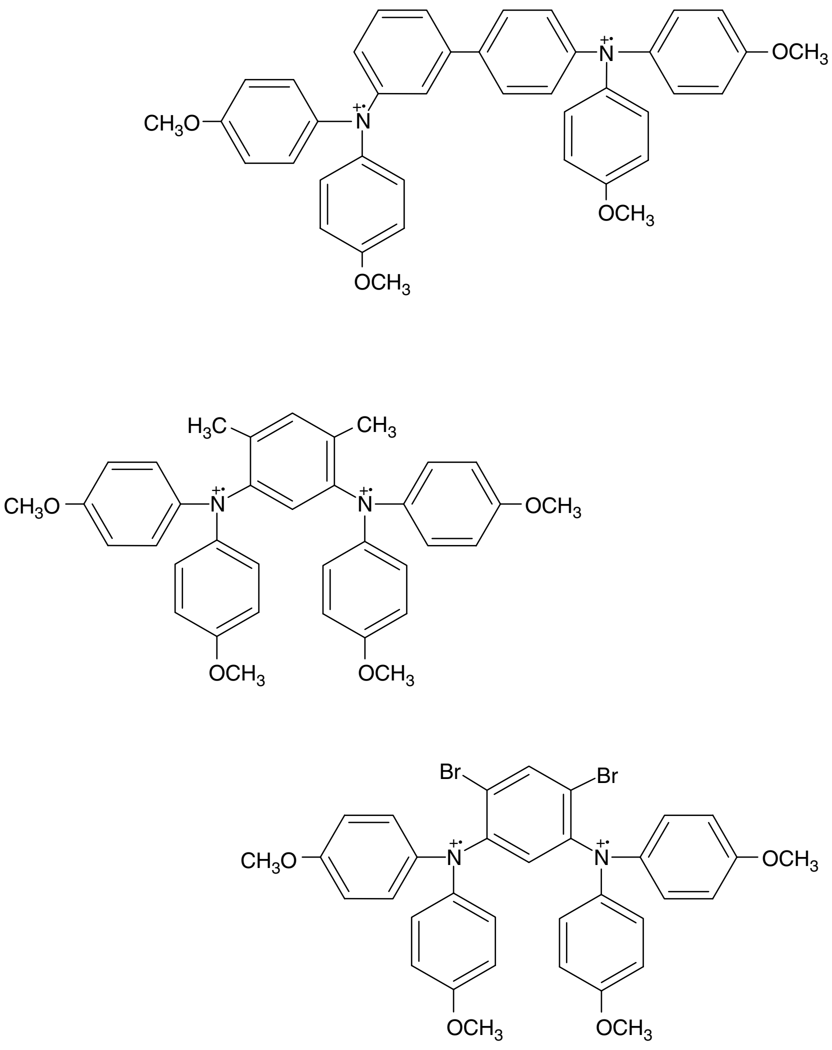
Wienk and Jansen (1996) have designed *N*,*N*′-bis[4-(diphenylamino)phenyl]-*N*,*N*′-diphenyl-1,3-diaminobenzene (Scheme 1.35).

The phenylaniline shown in Scheme 1.35 consists of alternating para- and meta-substituted phenylene (C_6H_4) rings to give the desired chemical stability from the *p*-diaminobenzene unit and ferromagnetic coupling from the *m*-diaminobenzene unit after two-electron oxidation. The *N*-phenylaniline oligomer depicted in Scheme 1.35 was oxidized with more than two equivalents of thianthrenium perchlorate to form the dication-diradical. The product is stable at room temperature and has a triplet ground state as evidenced from ESR spectroscopy. Using *N*,*N*′-bis(*p*-anisyl)-1,3-diaminobenzene or *N*,*N*′-bis(*p*-anisyl)-2,7-diaminonaphthalene as central units, Blackstock's group prepared the analogous dication-diradicals that were found to be solution-stable triplets (Stickley and Blackstock 1994, Selby and Blackstock 1999).

Depending on the amount of thianthreniumyl perchlorate, *N*,*N*,*N*′,*N*′,*N*″,*N*″-hexakis(anisyl)-1,3,5-triaminobenzene gives its cation-radical, dication-diradical, and trication-triradical as well (Stickley et al. 1997). These species are stable in methylene chloride at low temperatures (at 298 K, they can exist for several days). The dication-diradical and trication-triradical structures are paramagnetic and ferromagnetic (Sato et al. 1997). Within the dendrimer shown in Scheme 1.35, the interior phenylene-diamino groups are more easily oxidized than the peripheral arylamino groups. A partial surrounding shell is formed. This leads to a radial redox gradient in the molecular system (Stickley and Blackstock 1994, Selby and Blackstock 1999). Such systems are promising as building blocks in developing new organic materials having useful spin and magnetic properties (see Hirao et al. 2006).

From the materials just mentioned earlier, one can conclude that mutual meta orientation (meta through a benzene) of the spin-bearing moieties is an indispensable condition for the existence of triplet states in aromatic di- or tri-(cation-radical)s. However, in fact, these systems have both singlet and triplet forms, and the questions are about what is the difference in the corresponding energy and which state is more stable. Stability of the polyion-polyradicals is also a very important factor, especially in the sense of practical application. Let us consider several relevant examples.

1. N,N,N′,N′-*tetra*(p-*anisyl*)-*3*,*4*′-*diaminobiphenyl*. According to Scheme 1.36, *N*,*N*,*N*′,*N*′-tetra(*p*-anisyl)-3,4′-diaminobiphenyl gives a dication-diradical on being oxidized with dichlorodicyanobenzoquinone in trifluoroacetic acid. The dication-diradical is stable in the solution at room temperature. Studies by cyclic voltammetry and ESR spectroscopy led to the conclusion that the two centers are not wholly independent and there is some "leakage" of charge and spin between the two halves (Bushby et al. 1997a, 1997b). Hence, the charge and spin distributions lead to substantial overlap. This statement finds its confirmation in cases of other similar systems (Karafiloglou and Launay 1998, Boman et al. 1999, Coropceanu et al. 2002). As seen, the system considered does not completely meet the meta rule.

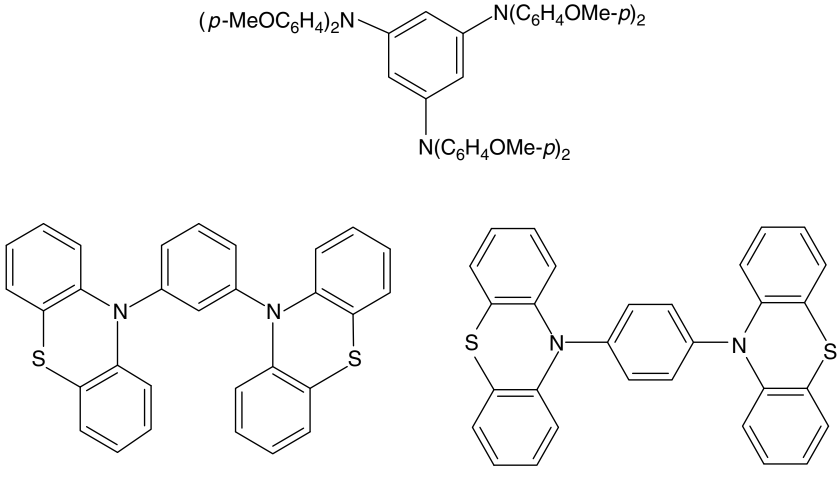


SCHEME 1.36

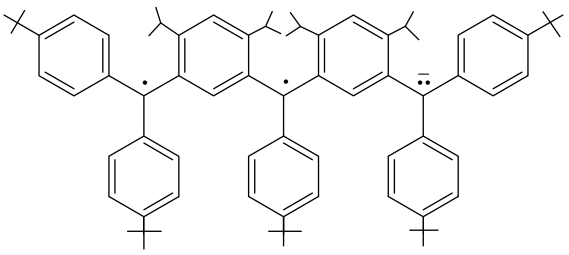
2. N,N,N′,N′-*tetra*(p-*anisyl*)-*1,3-phenylenediamine derivatives.* Being oxidized with antimony pentachloride in dichloromethane, the dimethyl or dibromo derivative forms dication-diradicals (Yano et al. 2007). Scheme 1.36 depicts their structures. No leakage of charge and spin takes place in these two species, but they extremely differ in stability. The dimethyl derivative decomposes (probably via the cleavage of the π conjugation). Surprisingly, the dibromo derivative is extremely stable although bulkiness of the bromo-substituent is comparable with the methyl group, and hindrances to the π conjugation in this species are the same. From the point of design of new magnetic materials, it would be very substantial to elucidate the role of the bromo group in stabilization of poly(ion-radical)s.
3. *Phenothiazine derivatives.* Comparison of the structures in Scheme 1.37 can lead to a prediction that hexa(anisyl)-1,3,5-triaminobenzene is more similar to 10,10′-(1,3-phenylene) diphenothiazine than to 10,10′-(1,4-phenylene)diphenothiazine. Nevertheless, on one-electron oxidation, these two isomeric diphenothiazines give dication-diradicals (Okada et al. 1996, Sun et al. 2004). As shown, *m*-phenylenediphenothaizine has a singlet state, and *p*-phenylenediphenothiazine has a triplet state. Both diphenothiazine dication-diradicals

> have nearly perpendicular geometries between the plane of the central phenylene ring and the thiazine moieties (Baumgarten 1997, Terada et al. 2005). A large dihedral angle certainly decreases the energy gap between the two SOMOs by breaking the π network. In the para isomer, the orbital interaction through the σ bonds is weaker than in the meta counterpart: Spin sources are separated by the longer chain of five bonds in the para isomer compared to the chain of four bonds in the meta isomer. In these geometries, mixing with σ orbitals of the central benzene ring destabilizes local cation-radical orbitals (Fang et al. 1995). For these reasons, the para isomer acquires the triplet state. The triplet state is crucial for the molecular magnetism, but it is disadvantageous in the sense of energy as compared to the singlet state. However, this disadvantage is compensated by the absence of electronic repulsion that is typical for singlets. Hence, the triplet state of the *p*-phenylene-bridged dication-diradical is more stable than that of the meta-bridged one.

If the extended *m*-phenylene structures have several spin-bearing centers, their triplet coupling depends on spatial spin distribution. The coupling degree is inversely proportional to r^3, where r is the distance between the "unpaired" electrons. Poly(arylmethyl) anion-diradicals exemplify such dependence (Rajca and Rajca 1995). When the charge (electron pair) is localized at the terminal site, as shown in Scheme 1.38, ESR studies indicate ferromagnetic coupling between the remaining "unpaired" electrons.



SCHEME 1.37



SCHEME 1.38

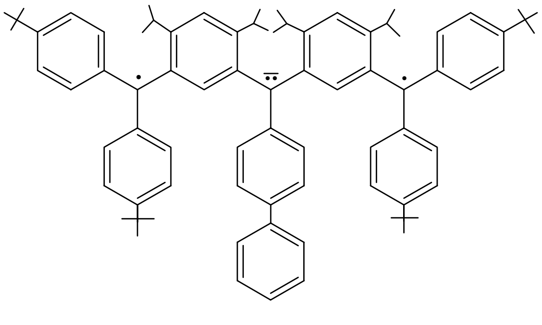
However, when the negative charge (electron pair) is localized at the center site, as shown in Scheme 1.39, antiferromagnetic coupling between the remaining “unpaired” electrons is observed.

The distance between the two spin-bearing centers is much greater in the structure shown in Scheme 1.39 than that shown in Scheme 1.38. Note that in this case, a control of spin coupling via control of electron localization is attained. The straightforward control of electron localization was implemented via modification of the substituents at the center site (compare Schemes 1.38 and 1.39). The mentioned anion-diradicals were prepared by partial oxidation of relative polyanions with iodine (Rajca and Rajca 1995). When the carbanion-stabilized 4-biphenyl, in the place of 4-*tert*-butylphenyl, was employed as a substituent at the center site, the negative charge was confined to the center site and the spin density to the terminal (nonadjacent) site.

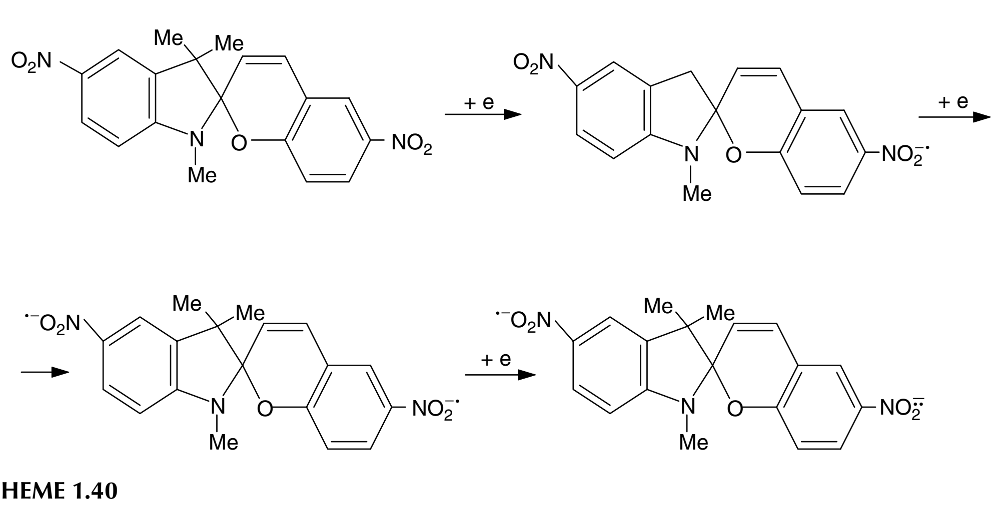
Control of charge/spin localization at the specific sites leads to two different kinds of spin coupling: (1) When spin sites are adjacent, spin coupling between the “unpaired” electrons is ferromagnetic. (2) When spin sites are not adjacent, because the pathway between them includes a site with negative charge (electron pair), spin coupling between the “unpaired” electrons appears to be antiferromagnetic.

Distribution of spin density in the framework of trianion-radicals allows determining whether or not there is some conjugation between substituents at different sites. For example, reduction of dinitro spiro(indoline-benzopyran) with potassium *tert*-butoxide in DMSO proceeds according to Scheme 1.40 (Alberti et al. 1995).

As shown by means of electrochemistry or ESR spectroscopy and confirmed by *ab initio* calculations (Alberti et al. 1995), the first electron is accommodated in the more accessible nitrobenzopyran moiety. The second electron fits into the nitroindoline moiety. The third extra electron is again



SCHEME 1.39



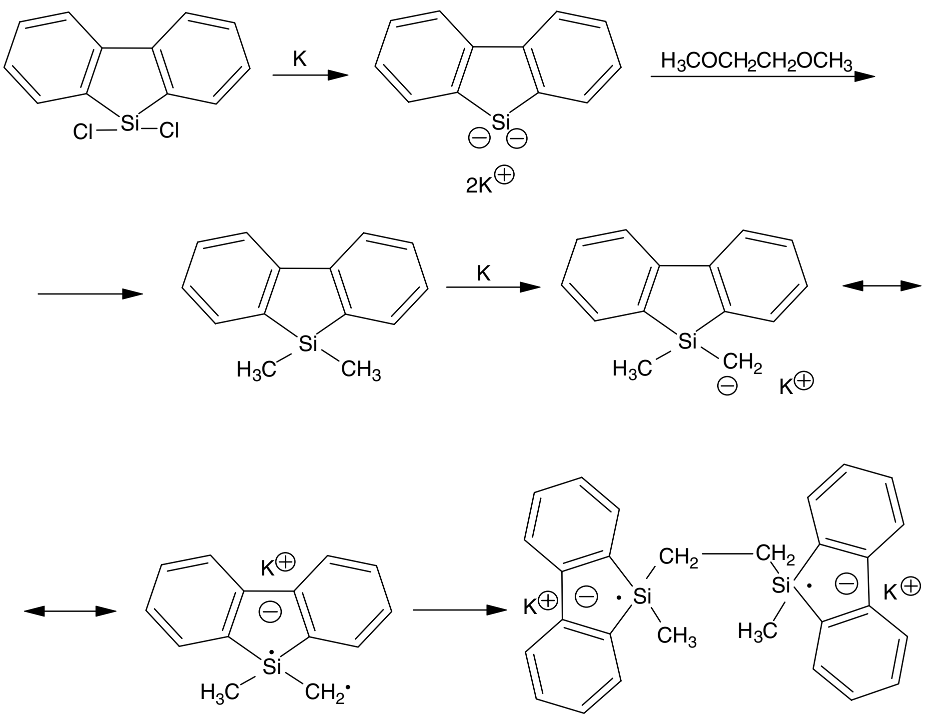
SCHEME 1.40

accommodated into the nitrobenzopyran unit without affecting the spin-density distribution on the opposite fragment. Hence, the spiro-nodal carbon atom prevents conjugative interactions between the indoline and benzopyran moieties.

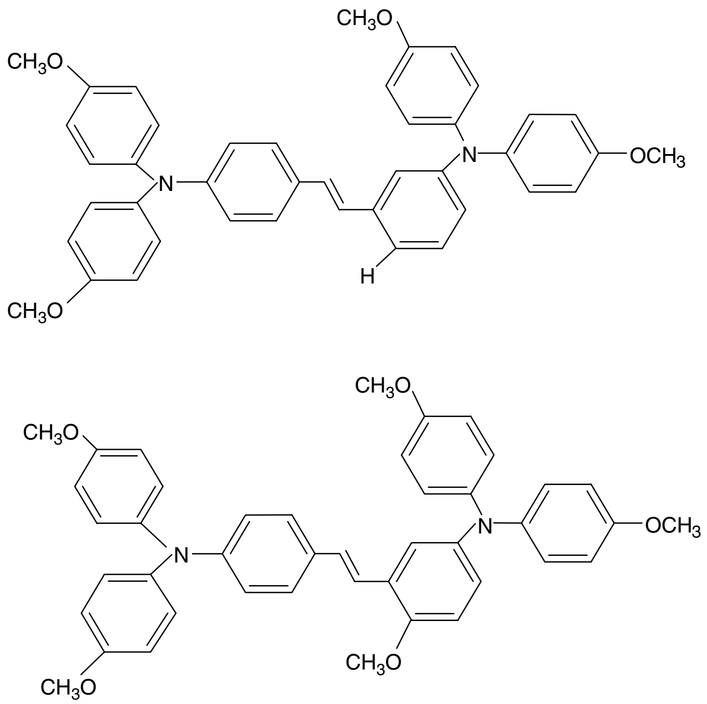
As mentioned earlier, low temperature and ion pairing favor the formation of poly(ion-radical)s. Surprisingly, the dianinon-diradical of bis(methylsilafluorenyl)ethane is formed after heating the silafluorene dianion dipotassium salt at 60–70°C for 12 h in DME containing hexane as cosolvent and 18-crown-6 ether as a potassium-cation complexing agent. This very unusual dianion-diradical was completely characterized by means of ESR spectroscopy and x-ray crystallography (Liu et al. 2002). Scheme 1.41 illustrates the formation and structure of this astonishing dianion-diradical; its remarkable stability can be explained by the availability of the vacant silicon *d* orbitals and the possibility for a single electron to be delocalized over two benzene rings fused with the silacyclopentadiene fragment. Indeed, x-ray data suggest the carbon–carbon bond alternation in the benzene rings and some loss of their aromatic character (Liu et al. 2002).

Scheme 1.42 marks out one additional and important aspect of ferromagnetic coupling in dication-diradicals. The stilbenoid compounds shown in Scheme 1.42 give $N^{+\bullet}\cdots/\cdots N^{+\bullet}$ dication-diradicals on two consecutive one-electron oxidations (anodic or by means of $NOPF_6$). The compound containing the methoxyl group in the stilbenoid fragment has a two-month half-life, even under ambient conditions. This half-life is five times longer than that of the counterpart with no methoxyl group in the stilbenoid moiety. However, introduction of the methoxyl group results in torsional twisting on the substituted stilbenoid framework. This weakens ferromagnetic coupling in the CH_3O-substituted dication-diradical as compared with the H (stilbenoid-unsubstituted) analog (Michinobu et al. 2001).

Therefore, ferromagnetic coupling is needed not only in the triplet orientation of the spins, but also in the spin-exchanging ability in the framework of a planar dication-diradical.



SCHEME 1.41



SCHEME 1.42

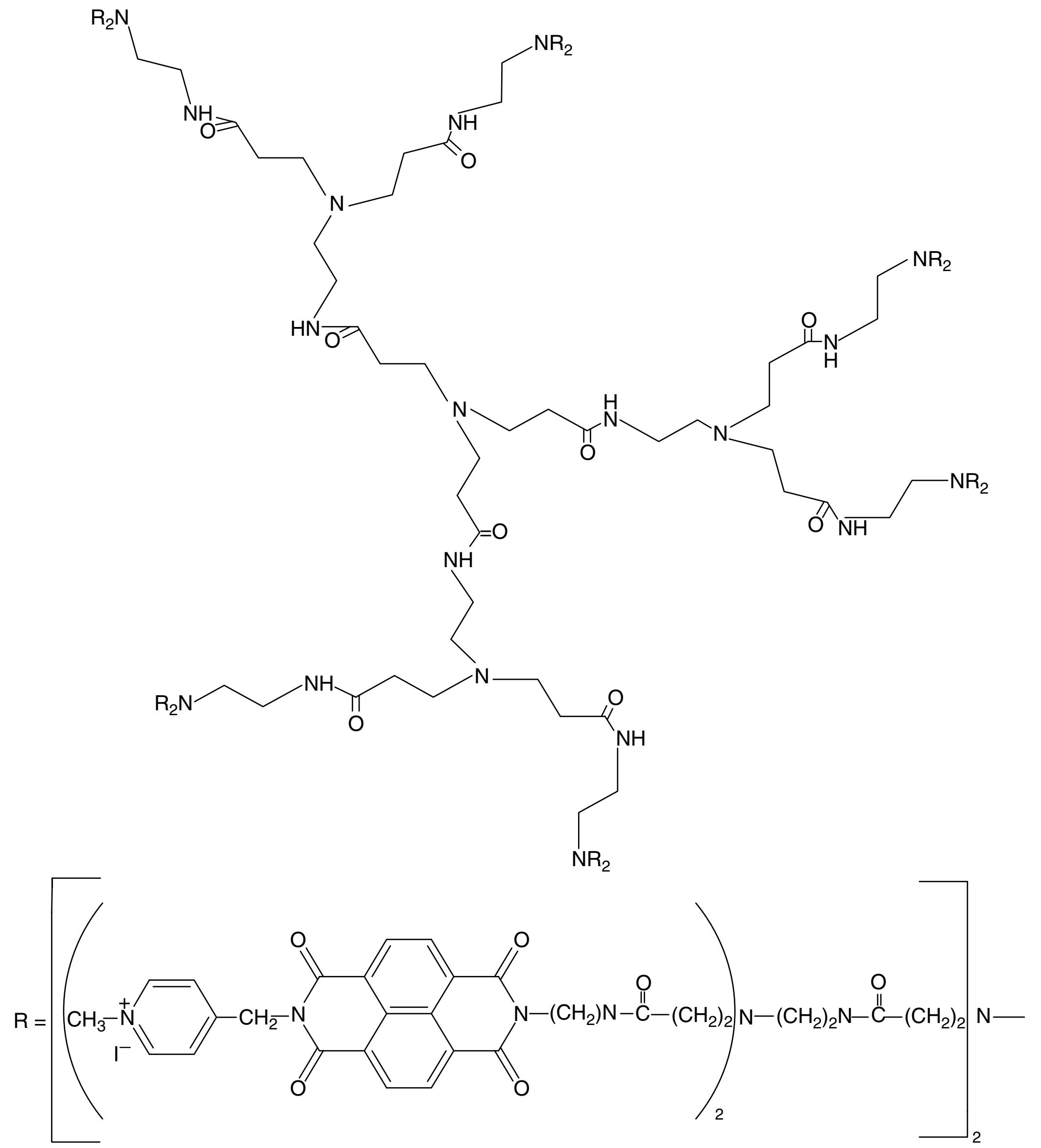
1.6 POLYMERIC ION-RADICALS

Polymeric ion-radicals are usually formed as a result of one-electron redox modifications of uncharged polymers containing electrochemically active groups. They attract an enhanced attention in the sense of possible practical applications. Because polymeric ion-radicals contain many spin-bearing groups, a similarity emerges between polymeric ion-radicals and poly(ion-radicals).

However, there is some specificity peculiar to polymers only. For example, $NOBF_4$ oxidation of the triphenylamine and diphenyltetraalkoxy fragments in a linear and networked polymer leads to the formation of cation-radical centers (Bushby et al. 1997b). As a rule, the quantity of ion-radical centers formed is low, not more than 10–20% of the theoretically possible values. This is a problem that is proving to be difficult to solve. A feasible explanation is that the effect is not electrostatic, but steric. There is a certain difficulty in accommodating large counterions within rather rigid polymer networks of bent polymeric chains.

Anion-radicals engrafted to hyperbranched polymers (dendrimers) deserve a special mention. Dendrimers are built-up by sequential synthesis of larger and larger generations, with branch points in each generation. The hyperbranched polymer chains cover the ion-radical centers and significantly suppress chemical side reactions, antiferromagnetic coupling, and through-space interactions. This covering also prolongs the ion-radical's half-life. Durability and the ground-state spin multiplicity of the reductively and oxidatively treated homo- or heteronuclear dendrimers are deemed technically promising.

In particular, poly(amidoamine) dendrimers were peripherally modified with diimide moieties (see the structure shown in Scheme 1.43). After reduction with dithionite, this dendrimer was cast into a film, the electronic properties of which were isotropic. (This means that on the molecular and macroscopic levels, there is a three-dimensional (3-D) electron delocalization.) The conductivity was humidity dependent. Water molecules integrate into the material's crystal structure and take part in long-distance electron transfer. Such an effect of water was also observed to enhance electric



SCHEME 1.43

conductivity of sodium cobalt oxide (Kuroki et al. 2007). At 95% humidity, a mixed-valence film (0.55 electron per diimide) showed electric conductivity at room temperature around 11 $\Omega^{-1}cm^{-1}$ (Miller and Mann 1996). Partially reduced, mixed-valence materials are required for organic metals of high electrical conductivity; this problem is the subject of a special consideration in section 8.3 devoted to organic metals.

The convergent synthesis of a range of aryl ester dendrimers with peripheral tetrathiafulvalene units was also reported (Devonport et al. 1998). The dendrimers acquire some amount of the cation-radical tetrathiafulvalene "tips" on reacting with iodine in solutions. Another promising material is polyphenylene dendrimers functionalized with benzophenone units. On being transformed into the potassium ketyl derivatives, the dendrimers bring forth intermolecular biradicals. These technically attractive species contain four-membered cycles that coordinatively combine two potassium cations

and two hydroxide functions of different dendrimeric molecules. Because the carbon-radical centers of metal ketyl fragments remain free, such intermolecular ion pairs acquire biradical properties (Bernhardt et al. 2005).

We have already pointed out that one of the main topics of modern interest in polymeric and oligomeric ion-radicals is the design of organic compounds with magnetic properties. Oligomers and polymers allow, in principle, the preparation of organic high-spin molecules. A well-established strategy is to connect neutral or charged radicals as spin-carrying units via organic linkers. These units may act as ferromagnetic coupling parts and provide the desired alignment of electron spins.

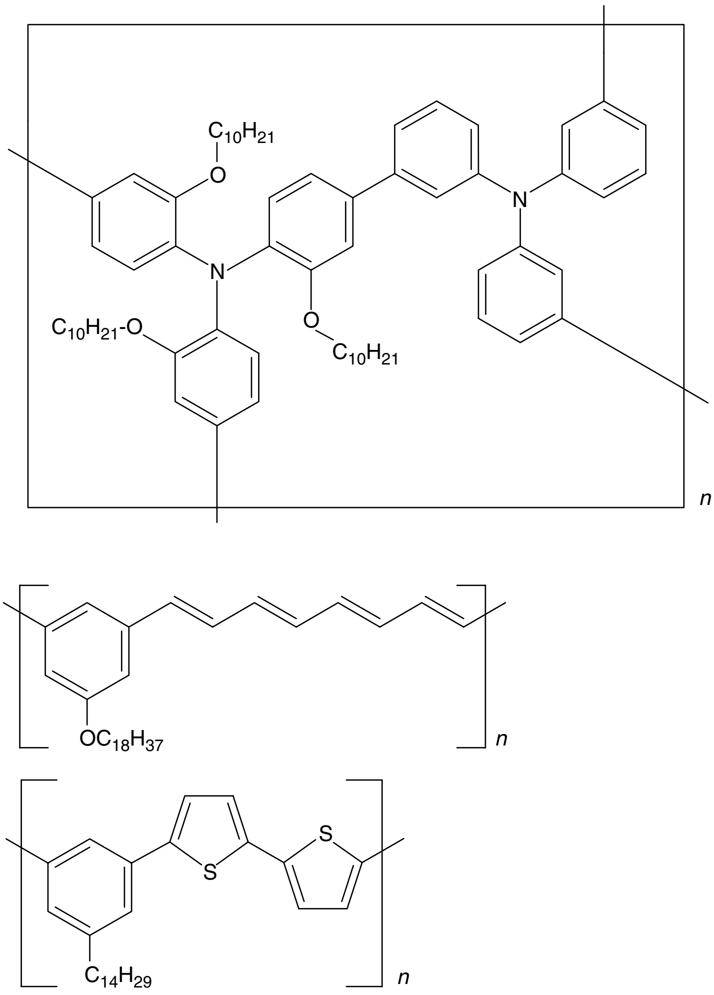
Polymeric ion-radicals often have *m*-phenylene, *m*-*p*-phenylene, or *m*-*p*-*p*-phenylene as a coupling unit, too (cf. Section 1.5). This unit couples ion-radical centers by an in-phase periodicity of the spin polarization. Cooperative interaction of a large number of unpaired electrons may eventually result in high-spin polymers (oligomers) and ultimately in ferromagnetic materials. Thus, oxidation of poly(*m*-*p*-aniline) by one equivalent of hexachloroantimonate creates mostly isolated cation-radicals. On action of 1.5 equivalent of the oxidizer, poly(cation-radical)s are generated in which ferromagnetic interaction was observed (Kulszewicz-Bajer et al. 2007). It should be noted that, in such cation-radicals, a ferromagnetic interaction caused by meta coupling dominates over an antiferromagnetic one realized by para coupling (Galecka et al. 2004). The ferromagnetic character of the interaction is very promising for fabrication of the magnets based on polyaniline polymers.

Meanwhile, an interesting approach toward para-conjugated high-spin poly(cation-radical)s was theoretically developed (Fukutome et al. 1987). This strategy aimed at construction on such ferromagnetic chain in which unpaired electrons can be introduced by oxidation of π-conjugated segments. Those cation-radicals were supposed to be positioned between the coupling units. In the language of solid-state physics, the cation-radical segments are polarons.

For instance, *p*-phenylene diamine oligomers have been successfully oxidized to high-spin ground-state oligo(cation-radical)s that are stable at room temperature (Stickley and Blackstock 1994, Stickley et al. 1997, Wienk and Janssen 1996, 1997). Ferromagnetic coupling occurs between *p*-phenylene diamine cation-radicals in regioregular-substituted π-conjugated chains between neighbors and possibly between next-nearest neighbors (Meurs and Janssen 2000, 2001, Yan et al. 2005) also. Based on ESR/ENDOR spectra and UB3LYP calculations, Grossmann et al. (2004) defined the situation precisely. The main portions of the spin and the charge are confined to the central phenylenediamine moiety. In other words, only a very limited electron delocalization into the adjacent phenyl substituents exists. Known electric conductivity of polyanilines (emeraldine salts) are predominantly caused by "soliton hopping" between different polymeric chains, neighboring in stacks. This process proceeds in 3-D space, rather than one-dimensional (1-D) soliton-conducting chains.

Poly[(aniline-2-chloroaniline)-4-toluenesulfonic acid salt] was obtained by oxidative copolymerization of aniline with 2-chloroaniline in solutions containing 4-toluenesulfonic acid. The copolymer salt was subjected to heat treatment under nitrogen atmosphere at elevated (about 150°C) temperatures. The heat-treated samples acquired electric conductivity of $2.7 \times 10^{-2}\ \Omega^{-1}\text{cm}^{-1}$. According to ESR spectra, the heated poly[(aniline-2-chloroaniline)-4-toluenesulfonic salt] exists as the poly(semiquinone imine ion-radical) in which unpaired electrons are localized on or near the nitrogen atoms (Palaniappan 1997).

Yakuphanoglu and Senkal (2007) proposed the following chemical step for the preparation of polyaniline-containing cation-radical segments. Aniline and methylsulfonic acid react to form anilinium methylsulfonate. This salt is placed in ionic liquid prepared from trioctylamine and methylsulfonic acid. Both the ammonium salts are mixed and treated with dibenzoyloxide. The mixture, on being poured into hexane, expels a polymer. The polymer which is rid of the solvent is easily dissolved in DMF, methylpyrrolidone, DMSO, or acetone and can be used as a filmlike electrolyte material, the so-called polymer electrolyte. The electric conductivity of the polyaniline prepared in ionic liquid ($2.1 \times 10^{-1}\ \Omega^{-1}\text{cm}^{-1}$) is higher than that of polyaniline prepared by other



SCHEME 1.44

methods: 9.11 × 10^{-4} $\Omega^{-1}cm^{-1}$ (Yan et al. 2002), 5.3 × 10^{-4} $\Omega^{-1}cm^{-1}$ (Devendrappa et al. 2006), and 7.5 × 10^{-2} $\Omega^{-1}cm^{-1}$ (Palaniappan 2002).

The polaronic strategy has also been applied to polymers, incorporating *m*-phenylene units as coupling links in π-conjugated polymer chains of poly(thienylene ketone) (Dal Colle et al. 1999) as well as of polyarylamine, polyacetylene, and polythiophene (Kaisaki et al. 1991, Murray et al. 1994, Bushby et al. 1997a). Scheme 1.44 represents these polaronic polymers.

Oxidation of the polymers from Scheme 1.44 leads to the polymeric cation-radicals with ferromagnetic coupling of spins. Surprisingly, however, the spin concentration in these polymer networks was extremely low. A small percentage of the cation-radical units actually carried an unpaired electron. Several explanations were proposed for this disappointing result. As it has already been noted, for the cross-linked polymers, a more likely interpretation is the steric difficulty of incorporating counterions into a relatively rigid polymer network (Bushby et al. 1997b). The authors bear in mind the PF_6^- anion as the counterion to each cation-radical part of the cross-linked polymer. If it is so, this is unlikely to be insurmountable. A bulky anion can be replaced by an anion of small size.

As with the tailor-made polymers, a more serious, perhaps intrinsic, cause is discussed (van Haare et al. 1998). These polymeric cation-radicals form π macrodimers according to usual

equilibria $2M^{+\bullet} = (M)_2^{2+}$. The π dimerization inhibits the formation of high-spin states. Murata et al. (2004, 2005) proposed to construct homopolymers of the polyvinylene backbone bearing anisylaminiumyl side fragments as polarons. The neat samples of such polymers display both substantial chemical stabilities and multiplet states without any intermolecular reactions. These pendant-type high-spin poly(cation-radical)s possess the following merits:

1. Their π-conjugated backbone provides a ferromagnetic spin interaction over a long chain. The spins can interact not only with their neighboring spins, but also with more remote spins. This is very important because this interaction makes the spin coupling insensitive to the spin defect.
2. Diverse, chemically stable pedant polarons can be introduced into a polymer chain. The resultant poly(cation-radical)s are really stable and easily handled. They are described as monthly stable at room temperature in air! (Murata et al. 2004, 2005). These properties open a way to advanced applications of magnetic organic molecules in the future.

Charge transport in charge-injected polymers is extensively studied because of its importance in practice. Sometimes, it is sufficient to introduce a donor or an acceptor in a polymer. This leads to the formation of a charge-transfer complex, which transforms into an ion-radical salt on physical excitation. Thus, Lee et al. (1997) studied the photoconductivity of pyromellitic dianhydride-diaminodicyclohexylmethane polyimide, the electron acceptor, in the presence of *N*,*N*,*N*′,*N*′-tetramethyl-*p*-phenylenediamine, the electron donor. The addition of the electron donor increased the photocurrent generation of polyimide films by about three orders of magnitude. The polyimide from an alicyclic diamine doped with an electron donor showed even a larger enhancement of photocurrent. This occurs due to an intermolecular charge-transfer complexation. In the case of the aromatic polyimide, both inter- and intramolecular charge-transfer complexes can be formed. By and large, any enhancement of photocurrent by the electron donor is attributed to photoabsorption by the molecular charge-transfer complex formed between the added electron donor and pyromellitic imide unit of the polymer backbone. The photoexcitation provokes the rapid electron transfer from the donor to pyromellitic imide. This produces the anion-radical of polymer and the cation-radical of the donor, resulting in the photoconductivity in the bulk polyimide films.

Localization or delocalization of an excess electron (in anion-radicals) and a hole (in cation-radicals) along the polymer chain defines the electronic conductivity of the polymeric ion-radicals. From this point of view, it is correct to mention that the cation-radical oligomers are formed from octithiophene (Geskin et al. 2003) and vinylene-bridged octithiophene (Casado et al. 2000). The quantum-chemical calculation indicates localization of polaron around the middle of the chain. The same localization was indicated in the case of polypyrrole. A neutral polypyrrole in the ground state was shown to assume a helical shape. On oxidation, the chain becomes planar within the polaron, an effect due to enhanced interring π bonding (Lin et al. 2005).

Being initially heteroaromatic, α,ω-bis(mesylthio)oligothiophenes form charged species in which the conjugated path becomes quinoidal. Stable cation-radicals, dications, and even tri(cation-radical)s are generated on chemical oxidation of the initial materials by ferric chloride in dichloromethane. Longer chain lengths better stabilize higher oxidation states. α,ω-Sulfur atoms of α,ω-bis(mesylthio)oligothiophenes are actively involved in the formation of the charged species and exert a favorable tuning of their electronic structure. These features were established by means of electron absorption and Raman spectroscopy in combination with calculations in the framework of DFT (Casado et al. 2005).

Other representatives of polaronic polymers that are derived from polysilanes also attract significant technical interest. Polysilane is a 1-D σ-conjugated polymer. Generally, the silyl group can support electron transfer through low-lying *d* and σ* orbitals (see, e.g., Gherghel et al. 1995). Several scientific groups investigated the localization length (LL) of the electron/hole conduction in polysilanes. Irie and Irie (1997) and then, Seki et al. (2001) recorded the absorption spectra of

ion-radicals of polyalkylsilanes. The spectra had two peaks in the UV and near-infrared (NIR) regions, and the maxima of the peaks shifted to longer wavelengths with increasing chain length until about 16 monomer units and clearly showed saturation above this length (i.e., LL = 16). Kumagai et al. (1996) and Ichikawa et al. (1999) measured electron-spin resonance and the electronic absorption spectra of anion and cation-radicals derived from oligosilanes (up to six monomeric units) or from polysilanes (approximately 500 units). The spectra of the polymer ion-radicals were similar to those of the oligosilane ion-radicals. This suggested that both the excess electron and hole were not delocalized all over Si—Si main chain of the polymeric ion-radical. The excess electron and the hole in the polysilane ion-radical are confined to only a part of the polymer chain composed of six silicon atoms (LL = 6). Calculations within DFT confirms the following: For ion-radicals of permethylhexasilane, $Si_6(CH_3)_{14}^{\pm\bullet}$, the hole in the cation-radical and the electron in the anion-radical are really delocalized over the six-silicon skeleton (Tachikawa and Kawabata 2007a). Thus, the publications cited here point out that excess electrons and holes are localized on a few silicon atoms, although the LL reported in each work is slightly different.

Tachikawa (1999) and Acharya et al. (2005) also analyzed the mobility of carriers along the silicon chain. The results obtained should be mentioned separately. As it turned out, the mobility obtained for a positive charge (hole) was several times larger than that for an excess electron. This result suggests that the localization mechanism of a hole and that of an electron are different from each other. Probably, an excess electron is trapped in the defect of the main chain, whereas a hole is not trapped. The defects are mainly structural ones such as branching points and oxidized sites (Seki et al. 1999). This can lead to different electron conductivity. Moreover, effects of groups directly bonded to the silicon skeleton are also essential in this sense. The delocalization of the positive polaron state or SOMO proceeds more efficiently when phenyl rather than (or along with) alkyl groups are bonded to the silicon backbone chain (Seki et al. 2004, Tachikawa and Kawabata 2007a,b). This indicates the importance of σ–π mixing in intermolecular hole-transfer processes. Continuation of the polysilane ion-radical studies will hopefully result in some important technical applications.

1.7 INORGANIC ION-RADICALS IN REACTIONS WITH ORGANIC SUBSTRATES

Practically, every organic reaction proceeds with the indispensable participation of inorganic substances involved in redox processes. Among these species are oxygen, halogens, compounds of sulfur and nitrogen with oxygen, inorganic ions of the hydroxide type, and metallic ions. As a result of electron transfer, the inorganic ions are oxidized, reduced, or somewhat changed with respect to the oxidation state. Many of the electron-transfer reactions start from an attack of an organic substrate by an inorganic reactant. The latter often reacts in its ion-radical state (the $SO_4^{-\bullet}$ anion-radical is a typical example). Some ion-radical transformations of organic compounds take place with the assistance of active components in a gaseous medium (O_2, CO_2). These components can give rise to ion-radicals ($O_2^{-\bullet}$, $CO_2^{-\bullet}$).

Therefore, some concise review of the conditions of formation as well as physical and chemical properties of the most important inorganic ion-radicals is in order here. Special attention ought to be given to their reactions with organic compounds both in an initial uncharged form and in a postelectron transfer form. It is also very important to understand the difference between redox reactions of the same ions acting under different conditions of solvation—or why ions with close redox potentials are quite different in the sense of their activity in liquid-phase electron transfer. For example, Cu^{2+} ion is a weak oxidant in aqueous solutions. In AN solutions, the same ion is a rather strong oxidant (Ahrland et al. 1983). Ions NO^+ and NO_2^+ are close in their E^0 values (1.51 and 1.56 V, respectively; Cauquis and Serve 1968, Bontempelli et al. 1974). Nevertheless, these icons seriously differ in their oxidative strength, see section 1.7.10. There is a marked solvent dependence of the standard potential E^0 for the NO_2^+/NO_2 couple: 1.56 V in AN, 2.05 V in sulfolane, and 2.32 V in nitromethane (Boughriet and Wartel 1989a, 1989b). In other words, the oxidative properties of NO_2^+ depend on solvating capability.

On account of the weak solvation properties of nitromethane, the NO_2^+ species is found to be the more powerful oxidizing agent in nitromethane than in sulfolane and particularly in AN.

1.7.1 Superoxide Ion

The standard potential of the $O_2/O_2^{-\bullet}$ pair is equal to −0.15 V in water and −0.60 V in DMF. Usually, dioxygen easily captures two electrons in the stepwise reaction: $O_2 + e \rightarrow O_2^{-\bullet}$, then $O_2^{-\bullet} + e \rightarrow O_2^{2-}$. In DMSO, dioxygen reductions into the superoxide ion and then into the dioxygen dianion are characterized by $E_{1/2}^1 = -0.5$ V and $E_{1/2}^2 = -1.5$ V in regard to the saturated calomel electrode (Sawyer and Gibian 1979). The superoxide ion occupies an intermediate position in the following redox triad: $O_2 \rightarrow O_2^{-\bullet} \rightarrow O_2^{2-}$. In accordance with such a position, the superoxide ion possesses a dual reactivity: Depending on the substrate character, the ion can act as an acceptor and as a donor of one electron. For instance, the superoxide ion transfers one electron to quinone (Q) and transforms it into a semiquinone (SQ): $O_2^{-\bullet} + Q = SQ + O_2$. As it was found out, the direct and reverse processes are fast but have different rates: $k_1 = 1.1 \times 10^9$ and $k_{-1} = 10^7$ L $mol^{-\bullet 1}s^{-1}$ (Morkovnik and Okhlobystin 1979).

According to a widespread opinion, the superoxide ion possesses expressed oxidative properties. Thermodynamically, however, it must be a weak oxidant and a moderate strong reductant (Sawyer and Gibian 1979). This statement refers, of course, to aprotic mediums in which the superoxide ion is stable. In the presence of proton donors, the superoxide ion undergoes disproportionation according to the following sequence: $O_2^{-\bullet} + H^+ \rightarrow HOO^\bullet$ and $O_2^{-\bullet} + HOO^\bullet \rightarrow O_2 + HOO^-$.

Protonation enhances the electron affinity of the superoxide ion and it easily transforms into hydrogen peroxide: $HOO^- + H^+ \rightarrow H_2O_2$ (Costentin et al. 2007).

In all the aprotic solvents (with no proton donor admixtures), the superoxide ion generally cannot act as an oxidant, taking into account a wide range of functionally substituted compounds. For example, in dry pyridine, $O_2^{-\bullet}$ does not oxidize 1,2-dimethoxybenzene (Sawyer and Gibian 1979). This ion, however, reacts with 1,2-dihydroxybenzene. For the OH form, the first step consists of proton transfer from the hydroxyl group to the superoxide ion. Next, reactions proceed with the participation of $HOO^\bullet$. The literature on oxidation of hydrazines, thiols, and alcohols with the superoxide ion refers to reactions that begin from the formation of the $HOO^\bullet$ radical. It is significant, in this respect, that there are no reactions between the $O_2^{-\bullet}$ ion and dialkyl sulfides, dialkyl ethers (esters), or alcoholates. All of these substrates do not contain a labile proton. The free hydroperoxide radical ($HOO^\bullet$, which is formed from $O_2^{-\bullet}$ after the proton addition) is a conjugate acid of a base, that is, of the superoxide ion. This acid is rather strong, its $pK_a = 4.88$ (Sawyer and Gibian 1979). Hence, dissociation of the acid with the generation of a proton and a peroxide ion is possible even in acid media. However, the irreversible reaction between $HOO^\bullet$ and $O_2^{-\bullet}$ suppresses the dissociation. Studies in the chemistry of $O_2^{-\bullet}$ anion-radical have achieved noticeable success only during the past decades. Convenient preparative methods of electrochemical reduction of molecular oxygen were developed to obtain solutions of tetraalkyl ammonium superoxides in aprotic solvents. Usually, oxygen (in a gaseous stream through a phone electrolyte, Alk_4NX, solution) is electrolyzed at the controlled potential of −1 V. As solvents, DMF, DMSO, AN, and pyridine are employed. Mercury, platinum, and gold are used as cathodes. The colored solutions formed give an ESR signal at a low temperature. The signal corresponds to the superoxide ion.

A complete chemical method has been proposed to obtain the superoxide ion (Miyazawa et al. 1985). In this case, oxygen is bubbled through DMF, THF, DMSO, or CCl_4 solutions of the potassium or tetrabutyl ammonium salt of 4-benzyloxy-1-hydoxy-2,2,6,6-tetramethyl piperidine. The resulting products are 4-benzyloxy-2,2,6,6-tetramethyl piperidine-1-oxyl, KO_2, or $Bu_4N^+O_2^{-\bullet}$ in 90% yields. Alkali superoxides are slightly soluble in organic solvents. Their solubility can be described as moderate only in DMSO. However, in the presence of crown ether, the solubility of superoxide in DMSO becomes excellent. The same applies to benzene as a solvent (Morkovnik and Okhlobystin 1979). Another chemical reaction of oxygen giving a metal superoxide consists of a

single-electron transfer to oxygen from Fe^{I} sandwich cyclopentadienyl (Cp)-arene complexes in the presence of metal salts: $[CpFe^{I}Arene]^0 + O_2 \rightarrow [CpFe^{II}Arene]^+, O_2^{-\bullet}$ then $[CpFe^{II}Arene]^+, O_2^{-\bullet} + M^+, X^- = [CpFe^{II}Arene]^+, X^- M^+$, and $O_2^{-\bullet}$. In this sequence, the reversible reaction is shifted to the right when the metal-salt anion, X^-, is larger and the metal-salt cation, M^+, is smaller. For example, the shift to the right is 100% in the presence of Na^+ and PF_6^- and only 35% in the presence of Na^+ and F^- (Hamon and Astruc 1988). The equilibrium takes place as an exchange reaction between the two ion pairs. Reactions of this type are based on the symbiotic-effect premise: The interaction between a hard cation and a hard anion or between two soft ions is stronger than that between two ions of different types.

One method of chemical generation of the superoxide ion deserves a short description because of the simplicity of the reagents employed. The ion is generated from oxygen in aqueous alkaline solutions of sodium dithionite, $Na_2S_2O_4$. The concentration of $O_2^{-\bullet}$ ion in the oxygenated solutions depends on that of $SO_2^{-\bullet}$ at any moment of the reaction (Wang and Chen 1997). The latter anion-radical originates from the dithionite ion: $S_2O_4^{2-} = 2SO_2^{-\bullet}$. This anion-radical reduces oxygen: $2SO_2^{-\bullet} + O_2 \rightarrow 2SO_2 + O_2^{-\bullet}$.

The reaction of 1-hydroxy- or 1-aminonaphthoquinone with O_2 shows a significant feature of the superoxide ion formation. The superoxide ion forms a van der Waals complex with another product of this reaction, a semiquinone. Hydrogen bonds are formed between $O_2^{-\bullet}$ and the OH and NH_2 groups of the corresponding semiquinone. As a result, the reaction equilibrium is shifted to the right (Liwo et al. 1997).

1.7.1.1 Reactions of Superoxide Ion with Organic H Acids

The $O_2^{-\bullet}$ ion in a solution promotes proton abstraction from a substrate or a solvent. This results in the formation of organic bases, which are conjugated with the appropriate H acids. All H acids with a pK_a value lower than 23 can take part in such proton transfers (Sawyer and Gibian 1979). For this reason, even organic acids (HB), which are weaker than water, enter the exothermic reaction, namely, $HB + 2O_2^{-\bullet} \rightarrow O_2 + HOO^- + B^-$.

If HB is a weak acid, this reaction is rather slow, but it nevertheless takes place. Substances that are unable to react with $O_2^{-\bullet}$ can also be involved when the solvent–reactant mixtures contain water or other proton donor compounds, even in traces. Thus, benzaldehyde is absolutely resistant to the action of the superoxide ion. However, benzaldehyde transforms into benzylic alcohol and benzoic acid on the action of $O_2^{-\bullet}$ in the presence of moisture. Sawyer and Gibian (1979) described the following "superoxide" variant of the Cannizzaro reaction: $2O_2^{-\bullet} + H_2O \rightarrow O_2 + HOO^- + OH^-$ and $2PhCHO + OH^- + H_2O \rightarrow PhCOOH + PhCH_2OH$.

Proton-containing admixtures in a solvent or in benzaldehyde can act like water. The superoxide ion abstracts such labile proton and generates the HOO^- base. The base in its turn abstracts proton from a solvent, for example, AN. If benzaldehyde is present, it is converted into cinnamyl nitrile according to the following simple reactions:

$$PhCHO + {}^-CH_2CN + H^+ \rightarrow PhCH(OH)CH_2CN$$

$$PhCH(OH)CH_2CN \rightarrow H_2O + PhCH{=}CHCN$$

The treatment of benzaldehyde with potassium hydroxide in AN results in the formation of the same product, that is, cynnamyl nitrile (Sawyer and Gibian 1979).

Thus, in the presence of water or other proton sources, the $O_2^{-\bullet}$ ion forms HOO^-—the strong base. Therefore, many reactions that are ascribed to the superoxide ion are actually reactions with proton donors. These reactions produce effective oxidants (O_2 and $HOO^\bullet$) and strong bases (HOO^-, OH^-, or B^-). This route of base generation finds its applications in synthetic practice. Thus, ethyl

nitroacetate is a relatively strong acid (in H_2O, $pK_a = 5.75$; in DMSO, $pK_a = 9.2$). Reacting with $O_2^{-\bullet}$, this compound transforms into the corresponding carbanion required for several kinds of synthesis (Niyazymbetov and Evans 1993).

1.7.1.2 Reactions of Superoxide Ion with Organic Electrophiles

As noted earlier, the superoxide ion reacts with effective electron acceptors. It is a one-electron reductant of moderate strength. However, the superoxide ion can act as a nucleophile if a substrate has a decreased electron affinity. For instance, alkyl halides react with the ion: $O_2^{-\bullet} + RCH_2Hal \rightarrow RCH_2OO^\bullet + Hal^-$. This reaction initiates the next ones: $RCH_2OO^\bullet + O_2^{-\bullet} \rightarrow RCH_2OO^- + O_2$ and $RCH_2OO^- + RCH_2Hal \rightarrow RCH_2\text{–}OO\text{–}CH_2R + Hal^-$. Reactions of KO_2 with optically active alkyl halides proceed with the configurational inversion. Moreover, the reactivity changes in the same order as that of the usual S_N2 reactions (primary > secondary > tertiary; J > Br > Cl) (Sawyer and Gibian 1979).

Nevertheless, the S_N2 scheme does not exclude such a possibility of one-electron transfer: $RCH_2Hal + O_2^{-\bullet} \rightarrow [Hal^- \cdots RCH_2^\bullet \cdots O_2] \rightarrow RCH_2OO^\bullet + Hal^-$. This mechanism is quite probable since $O_2^{-\bullet}$ is an electron donor, and organyl halogenides can, in principle, accept one electron. With the one-electron mechanism, the inversion of configuration is determined with an $O_2^{-\bullet}$ attack on the side, which is opposite the halogen atom in RHal (Morkovnik and Okhlobystin 1979). The direction of this reaction depends on the nature of a solvent. In pyridine, benzene, and DMF, the main product is alkyl peroxide. In DMSO, an alkyl carbinol is the main product (Sawyer and Gibian 1979). Obviously, RCH_2OO^- reacts faster with the solvent Me_2SO than with the substrate RHal. The solvent addition takes place as follows: $RCH_2OO^- + Me_2SO \rightarrow MeS(O^-)(OOCH_2R)Me$. The subsequent decomposition of the adduct leads to the final alkylcarbinol in its anionic form: $MeS(O^-)(OOCH_2R)Me \rightarrow Me_2SO_2 + RCH_2O^-$.

Alkyl tosylates and mesylates are cleaved on the action of KO_2 in DMSO and give rise to the corresponding alcohols. This reaction also proceeds with inversion of configuration at carbon atoms (Morkovnik and Okhlobystin 1979). Such process may be of importance in prostaglandin chemistry.

Reactions of $O_2^{-\bullet}$ with esters $R^1C(O)OR^2$ also pass nucleophilic substitution as an initial step (Sawyer and Gibian 1979). Final products are acyl peroxides or carboxylic acids. The following set of equations explains the product formation:

$$R^1C(O)OR^2 + O_2^{-\bullet} \rightarrow R^1C(O)OO^\bullet + R^2O^-$$

$$R^1C(O)OO^\bullet + O_2^{-\bullet} \rightarrow R^1C(O)OO^- + O_2$$

$$R^1C(O)OO^- + R^1C(O)OR^2 \rightarrow R^1C(O)\text{–}OO\text{–}(O)CR^1 + R^2O^-$$

$$R^1C(O)\text{–}OO\text{–}(O)CR^1 + 2O_2^{-\bullet} \rightarrow 2R^1C(O)O^- + 2O_2$$

The reaction of superoxide ion with carbon tetrachloride is important for olefin epoxidations. This reaction includes the formation of the trichloromethyl peroxide radical: $O_2^{-\bullet} + CCl_4 \rightarrow Cl^- + Cl_3COO^\bullet$. The trichloromethyl peroxide radicals formed oxidize electron-rich olefins. The latter gives the corresponding epoxides. This peroxide radical is a stronger oxidizing agent than the superoxide ion itself (Yamamoto et al. 1986).

Hence, nucleophilic reactions of the superoxide ion are typical. This ion can be compared with the thiophenoxide and thiocyanate ions with respect to nucleophilicity. The cause of such high nucleophilicity lies in a so-called α-effect: In $^\bullet O\text{–}O^-$ ion, an attacking site (O^-) adjoins directly to a site ($O^\bullet$) with a significant electronegativity. This effect usually confers special activity to nucleophiles. The effect can be additionally enhanced by including the $O\text{–}O^-$ group in sulfenate,

sulfinate, or sulfonate molecules. One reaction of this kind can be exemplified as follows: $RSSR + O_2^{-\bullet} \rightarrow RSOO^\bullet + RS^-$ and $RSOO^\bullet + O_2^{-\bullet} \rightarrow RSOO^- + O_2$ (Oae et al. 1981).

Like the trichloromethyl peroxide radical, peroxothio compounds can perform even nucleophilic oxygenation of substrates that are inert to $O_2^{-\bullet}$ in aprotic solvents. For example, stilbene is not changed in dry benzene containing 18-crown 6-ether and KO_2. In the presence of diphenylsulfide, however, the interaction takes place and results in the formation of stilbene epoxide. According to Oae et al. (1981), stilbene initially gives $PhCH(OO^-)CH^\bullet Ph$ anion-radical adduct. Abstraction of $O^{-\bullet}$ from the adduct leads to stilbene epoxide with 40% yield (Oae et al. 1981).

To summarize, the superoxide ion has high basicity and nucleophilicity. It can react as a reducer and cannot serve directly as an oxidant.

1.7.1.3 Reactions of Superoxide Ion with Biological Objects

There are several enzymes that convert O_2 into $O_2^{-\bullet}$. The superoxide ion is produced in living organisms, especially in the respiration process (see the review by Tselinskii et al. 2001). Also, there are many indications that this anion-radical is particularly toxic to cells and can ultimately have deleterious effects on the health and well-being of certain individuals (see reviews by Lang and Wagnerova [1992] and Faraggi and Houee-Levin [1999]). Moreover, the hydroxyl radical (which can be formed from $O_2^{-\bullet}$ by the well-known Haber–Weiss reaction) also has very high toxicity (Sies 1986). The superoxide ion generally does not appear to be intrinsically bactericidal (Hurst 1997). However, phagocytic cells have the capacity to enzymatically generate $NO^\bullet$. Nitric oxide is also not bactericidal at physiologically relevant concentration levels, but reacts very rapidly with $O_2^{-\bullet}$ to form the peroxonitrite ion (ONO_2^-). (The bimolecular rate constant for this reaction is the largest recorded for any reaction of $O_2^{-\bullet}$ [Huie and Padmaja 1993].) The peroxonitrite ion is a powerful, relatively long-lived oxidant with marked bactericidal capabilities (Hurst 1997). Another route of superoxide anion-radical transformation lies in its dismutation on superoxide dismutase catalysis ($2O_2^{-\bullet} + 2H^+ \rightarrow O_2 + H_2O_2$).

Metal cations are present in many biological objects, and $O_2^{-\bullet}$ is known to coordinate with the metal yielding the corresponding complex. The binding energies of $O_2^{-\bullet}$ with divalent metal ions (including biologically important Mg^{2+}) have been determined as 0.5–0.7 eV (Fukuzumi and Ohkubo 2000). Being bonded into the complex, the metal cation is reduced easily, at more positive potentials. This means that O_2, the most important biological oxidant, can really act as a catalyst rather than as an oxidant in the biological reaction of electron transfer (see Fukuzumi et al. 2001).

1.7.1.4 Superoxide Ion–Ozone Anion-Radical Relation

Ozone is a metastable compound, and its decay to yield atomic and molecular oxygen requires the activation energy of ca. 105 kJ mol^{-1}. However, the ozone anion-radical in its turn splits up even more readily. Successful alkene ozonolyses are probably initiated by alkene-catalyzed decomposition of O_3. Some reversible single-electron transfer to O_3 is possible as a first weakly endothermic step. The ozone anion-radical initially formed is the extremely reactive species and should oxygenate alkene cation-radical very quickly and exothermally through mono-oxygen exchange. This process releases the superoxide ion (Schank et al. 2000, reference therein): $>C{=}C< + O_3 \rightarrow >C^+{-}^\bullet C< + O_3^{-\bullet} \rightarrow >C^+{-}C(O^\bullet)< + O_2^{-\bullet}$. Depending on the alkene cation-radical nature, open-chain oxygenation and epoxidation as well as the formation of other trivial ozonolysis products take place.

Alkylaromatic compounds are also oxidized by ozone according to the ion-radical mechanism (Galstyan et al. 2001). In acetic acid solution, ethylbenzene undergoes the ozone attack on the ring (80%) and on the alkyl group (20%). The presence of cobalt diacetate in the acetic acid medium protects the aromatic rings in nitrotoluene isomers from the ozone attack and directs the reaction practically entirely to the methyl groups. The corresponding nitrobenzoic acids are formed with the practically quantitative yields (Galstyan 2006). According to kinetic studies, the ozone consumption obeys the chain law (Galstyan et al. 2001).

The first of the reaction steps in the amine–ozone interaction also consists of one-electron transfer from the amine to ozone, with the formation of the corresponding cation and anion-radicals. The ozone anion-radical has been revealed at low temperatures. Formation of the superoxide ion and the amine nitroxide are the understandable results of the reaction (Razumovskii and Zaikov 1984, reference therein).

1.7.2 Atomic Oxygen Anion-Radical

There are transformations of organic oxygen-containing ion-radicals, which develop through the elimination of the atomic oxygen anion-radical. An example of such a transformation is the stilbene epoxidation mentioned earlier. The atomic oxygen anion-radical becomes an acting species when hydrogen peroxide or some other source of hydroxy radicals is employed in water mediums with pH >12 (Vieira et al. 1997). Therefore, properties of atomic oxygen anion-radical should be described, albeit concisely.

In reactions with organic substrates, the $O^{-\bullet}$ anion-radical is usually bad at electron transfer, but good at hydrogen atom abstraction. Because of the $O^{-\bullet}$ spherical symmetry, its reactions are vulnerable by steric factors. Because of the $O^{-\bullet}$ charged nature, its reactions with organic ions are of course susceptible to the effects of coulombic interaction also. Armstrong et al. (2004) showed that the predominant reactions with the anions of alanine and methylalanine proceed as follows:

$$O^{-\bullet} + H_2N\text{–}CH(CH_3)\text{–}CO_2^- \rightarrow HO^- + H_2N\text{–}{}^\bullet C(CH_3)\text{–}CO_2^-$$

$$O^{-\bullet} + H_2N\text{–}CH(CH_3)\text{–}CO_2^- \rightarrow HO^- + {}^\bullet HN\text{–}CH(CH_3)\text{–}CO_2^-$$

$$O^{-\bullet} + H_2N\text{–}C(CH_3)_2\text{–}CO_2^- \rightarrow HO^- + {}^\bullet HN\text{–}C(CH_3)_2\text{–}CO_2^-$$

Addition of $O^{-\bullet}$ to double bonds and to aromatic systems was found to be quite slow. Simic et al. (1973) found that $O^{-\bullet}$ reacts with unsaturated aliphatic alcohols, especially by H-atom abstraction. As compared to $O^{-\bullet}$, $HO^\bullet$ reacts more rapidly (by two to three times) with the same compounds. In the case of 1,4-benzoquinone, the reaction with $O^{-\bullet}$ consists of the hydrogen double abstraction and leads to the 2,3-dehydrobenzoquinone anion-radical (Davico et al. 1999, references therein). Christensen et al. (1973) found that $O^{-\bullet}$ reacts with toluene in aqueous solution to form benzyl radical through an H-atom transfer process from the methyl group. Generally, the $O^{-\bullet}$ anion-radical is a very strong H-atom abstractor, which can withdraw a proton even from organic dianions (Vieira et al. 1997).

It is important to emphasize that the atomic oxygen anion-radical plays a role in catalytic oxidation occurring on various oxide surfaces. For instance, $O^{-\bullet}$ reacts with methane at room temperature over various metal oxides (Lee and Gralowsky 1992). On solid catalysis, $O^{-\bullet}$ is more reactive toward alkanes and alkenes than other ionic oxygen species. Iwamoto and Lunsford (1980) assumed that $O^{-\bullet}$ is the active oxygen species oxidizing benzene to phenol on V_2O_5/SiO_2 with 70% selectivity at 10% conversion. The product is formed only on oxide surfaces, before leaving the solid (Azria et al. 1988). Dong et al. (2005) used a microporous material $[Ca_{24}Al_{28}O_{64}]^{4+} \cdot 4(O^{-\bullet})$ as a catalyst in the one-step synthesis of phenol from benzene in the presence of water. In this case, the benzene conversion reaches 30% and phenol selectivity approximately 90%. Active $O^{-\bullet}$ plays a crucial role in the formation of phenol by hydroxylating the benzene aromatic ring. The catalyst microporous composition is favorable for encaging abundant atomic oxygen anion-radicals (Hayashi et al. 2002).

1.7.3 Molecular Oxygen Cation-Radical

Although oxygen has a very high oxidation potential (4.7 V), it can be oxidized to $O_2^{+\bullet}$ under special conditions, for example, by means of ultramicroelectrode techniques (Cassidy et al. 1985). This cation-radical is of course a very strong oxidant. Its stabilized forms are $O_2^{+\bullet}SbF_6^-$ and $O_2^{+\bullet}AsF_6^-$. Presently, however, these salts are not considered as containing the oxygen

cation-radical. Although textbooks (e.g., Cotton and Wilkinson 1988, p. 462) describe $O_2^{+\bullet}$ as a firmly established ionic form of oxygen,

> this is based on the characteristics of O_2MF_6 (M = P, As, Sb, or Pt) and the assumption that these compounds are salts $[(O_2^{+\bullet})MF_6^-]$. Such an ionic formulation is inconsistent with the ionization potentials, electron affinities, and electronegativities of the constituent atoms. The more accurate description of O_2MF_6 molecules is a covalent adduct $(^\bullet OOF)M^YF_5$. (Sawyer 1991)

In any event, O_2SbF_6 and O_2AsF_6 act as very effective one-electron oxidants with regard to aromatic amines, nitrogen- and sulfur-containing heterocyclic compounds (Dinnocenzo and Banach 1986, 1988, 1989) as well as to perfluorobenzene, benzotrifluoride, and perfluoronaphthalene (Richardson et al. 1986). The oxidation proceeds in Freon ($CHClF_2$) at temperatures from −115 to −145°C, and the formation of the organic cation-radicals has been firmly established.

1.7.4 Carbon Dioxide Anion-Radical

Carbon dioxide, CO_2, is a typical component of the gaseous environment for reactions in air or in the presence of air traces. Therefore, both interactions between CO_2 and organic ion-radicals as well as reactions of $CO_2^{-\bullet}$ with uncharged molecules of organic compounds should be considered. Interaction of CO_2 with organic anion-radicals leads, as a rule, to carboxylic acids; $CO_2^{-\bullet}$ anion-radicals are not formed. Even such a one-electron reductant as the superoxide ion (in aprotic medium) simply adds to carbon dioxide: $CO_2 + O_2^{-\bullet} \rightarrow {}^\bullet OO{-}CO_2^-$. The additional product accepts an electron: ${}^\bullet OO{-}CO_2^- + O_2^{-\bullet} \rightarrow O_2 + {}^-OO{-}CO_2^-$. The total result consists of the formation of an aprotic equivalent of peroxycarbonic acid (Sawyer and Gibian 1979).

Vacuum UV irradiation of aqueous solutions containing formate is one of the methods to generate $CO_2^{-\bullet}$. Under such conditions, the carbon dioxide anion-radical is formed in the excited state. The excited anion-radical transfers an unpaired electron to nitrobenzene, benzoic acid, or benzaldehyde (Rosso et al. 2000).

Under conditions of γ-radiolysis, water (and water solutions) in air produces carbon dioxide anion-radicals: $H_2O \rightarrow H^\bullet + {}^\bullet OH + e_{aq}$ and $e_{aq} + CO_2 \rightarrow CO_2^{-\bullet}{}_{aq}$. The latter anion-radical is also formed in a reaction of the hydroxyl radical with formic acid or formate: ${}^\bullet OH + HCO_2^- \rightarrow H_2O + CO_2^{-\bullet}$ (Flyuht et al. 2001). This reaction is used to strictly ensure the reducing ability of radiolytic processes. Thus, pulse radiolysis of argon-saturated water generates both oxidizing (hydroxyl radical) and reduced (electron and atomic hydrogen) species. To attain reducing conditions exclusively, formate needs to be added. Formate scavenges the hydroxyl radical, giving the carbon dioxide anion-radical and water (El-Agamey et al. 2006). The ${}^\bullet OH$ oxidizer is removed from the reaction sphere.

Carbon dioxide itself can accept e_{aq} during radiolysis of water, giving rise to the carbon dioxide anion-radical. This anion-radical can add to carboradicals. Thus, aliphatic alcohols react with the radiolytically generated hydroxyl radicals, rupturing their C–H bonds: $RCH_2OH + {}^\bullet OH \rightarrow H_2O + RCH^\bullet OH$. These radicals accept the radiolytically generated $CO_2^{-\bullet}$ forming α-hydroxycarboxylic acids: $RCH_2OH + CO_2^{-\bullet} \rightarrow RCH(OH)COO^-$ (Morkovnik and Okhlobystin 1979).

Park et al. (2005) proposed another, pure-chemical and handy, method of the $CO_2^{-\bullet}$ generation comprising treatment of the sodium formate and persulfate mixture in DMF at 50°C: $S_2O_8^{2-} \rightarrow 2SO_4^{-\bullet}$ and $SO_4^{-\bullet} + HCOO^- \rightarrow HSO_4^- + CO_2^{-\bullet}$.

Another pure-chemical route to the generation of the carbon dioxide anion-radical is the reduction of hydrogen peroxide with Ti^{3+} in the presence of formate ions (Morkovnik and Okhlobystin 1979): $Ti^{3+} + H_2O_2 \rightarrow Ti^{4+} + {}^\bullet OH + {}^-OH$ and ${}^\bullet OH + HCOO^- \rightarrow H_2O + CO_2^{-\bullet}$.

The solvated $CO^{-\bullet}$ anion-radical has been observed and well characterized by ESR spectroscopy (Knight et al. 1996, Holroyd et al. 1997). Being solvated, $CO^{-\bullet}$ anion-radical forms complexes that yield quasifree electrons on photoexcitation. Gas-phase experimental studies (Saeki et al. 1999) and *ab initio* calculations (Tsukuda et al. 1999) indicate that static ion-dipole interactions stabilize

the $[(CO_2)_{n-m}(ROH)_m]^{-\bullet}$ type small clusters. In supercritical carbon dioxide, monomers and dimers of water, AN, and alcohols also form metastable complexes (Shkrob and Sauer 2001a, 2001b). Such complexation should be taken into account in studies of electron-transfer kinetics in reactions with participation of $CO_2^{-\bullet}$.

Considering methods of $CO_2^{-\bullet}$ generation, we partly broached a subject of its chemical reactivity. However, some important data should be added. Disproportionation of $CO_2^{-\bullet}$ leads to carbon monoxide and a carbonate, whereas dimerization results in the formation of oxalate (see the left and right directions of the following dual equation): $^{-}O_2C{-}CO_2^{-} \leftarrow 2CO_2^{-\bullet} \rightarrow CO_3^{2-} + CO$ (Morkovnik and Okhlobystin 1979).

The carbon dioxide anion-radical usually plays the role of a one-electron reductant; in DMF its $E^0 = -1.97$ V (Amatore and Saveant 1981). In the gas phase, solitary $CO_2^{-\bullet}$ loses one electron with an exothermic effect of ca. 45 kJ mol^{-1} (Compton et al. 1975).

Interactions of $CO_2^{-\bullet}$ with alkyl halogenides include dissociative electron transfer and nucleophile addition (Otero et al. 2006): $CO_2^{-\bullet} + RHal \rightarrow CO_2 + R^\bullet + X^-$ and $CO_2^{-\bullet} + R^\bullet \rightarrow$ R–COO$^-$.

The carbon dioxide anion-radical was used for one-electron reductions of nitrobenzene diazonium cations, nitrobenzene itself, quinones, aliphatic nitro compounds, acetaldehyde, acetone and other carbonyl compounds, maleimide, riboflavin, and certain dyes (Morkovnik and Okhlobystin 1979). The double bonds in maleate and fumarate are reduced by $CO_2^{-\bullet}$. The reduced products, on being protonated, give rise to succinate (Schutz and Meyerstein 2006). The carbon dioxide anion-radical reduces organic complexes of Co^{III} and Ru^{III} into appropriate complexes of the metals(II) (Morkovnik and Okhlobystin 1979). In particular, after the electron transfer from this anion radical to the pentammino-*p*-nitrobenzoato-cobalt(III) complex, the Co(III) complex with the *p*-nitrophenyl anion-radical fragment is initially formed. The intermediate complex transforms into the final Co(II) complex with the *p*-nitrobenzoate ligand.

$$CO_2^{-\bullet} + [O_2NC_6H_4COOCo^{III}(NH_3)_3]^{2+} \rightarrow CO_2 + [^{\bullet-}O_2NC_6H_4COOCo^{III}(NH_3)_3]^{+} \rightarrow [O_2NC_6H_4COOCo^{II}(NH_3)_3]^{+}$$

Hence, despite the presence of the central atom Co^{III}, an initial-electron transfer is directed not to this center, but to the *p*-nitrophenyl fragment. Obviously, this fragment, and not Co^{III}, provides an orbital, which is symmetrically appropriate and low-lying. A similar situation occurs in a reductive cleavage of arylsulfonic salts (see Chapter 3).

A double bond can react with $CO_2^{-\bullet}$ (Morkovnik and Okhlobystin 1979); the following equation represents one typical example:

$$CO_2^{-\bullet} + R^1R^2C{=}NOH \rightarrow R^1R^2C(COO^-)NHO^\bullet$$

As seen, the transformation into the anion-radical is a very effective way to activate carbon dioxide.

1.7.5 Carbonate Radical

This anion-radical is generated as a result of interaction between hydrogen carbonate and hydroxyl radical, often in conditions of biological transformations. The reaction is as follows: $HCO_3^- + HO^\bullet \rightarrow H_2O + CO_3^{-\bullet}$. Shkrob (2002) reviewed the earlier data on the structure and properties of $CO_3^{-\bullet}$. Properties of this anion-radical are mostly defined by its protonation: $H^+ + CO_3^{-\bullet} = HCO_3^\bullet$. High-level *ab initio* calculations by Armstrong et al. (2006) show that $HCO_3^\bullet$ is a strong acid with $pK_a = -4.1$, and $E^0(CO_3^{-\bullet}/CO_3^{2-}) = 1.23 \pm 0.15$ V. Being a highly oxidizing species, $CO_3^{-\bullet}$ is very active in bioorganic reactions. As shown, $CO_3^{-\bullet}$ causes oxidative damage to copper or zinc superoxide dismutase, SOD1 (Ramirez et al. 2005). In the presence of cysteine, however, the carbonate anion-radical can stimulate SOD1 peroxidase activity (Karunakaran et al. 2005).

Carbonates are widely used as buffers in organic redox reactions, and the formation of $CO_3^{-\bullet}$ should be taken into account in interpretation of their mechanisms. There are promising reports on $CO_3^{-\bullet}$ as a potential oxidant for the environmental-friendly delignification of pulp (Stenman et al. 2003, Carlsson et al. 2006).

1.7.6 Sulfur Dioxide Anion-Radical

The couple $SO_2/SO_2^{-\bullet}$ is characterized by $E^0 = -0.26$ V (in water; Bradic and Wilkins 1984). Such potential falls into the region of redox-protein activity. This suggests that the known damaging action of gaseous SO_2 does not correspond to the sulfuric acid formation, but is stipulated by SO_2 participation in biological electron transport. Sulfurous acid (i.e., $SO_2 + H_2O$) also causes detrimental effects by irritating the mucous membranes. Interestingly, the resistance of different organisms to sulfur dioxide correlates with the relative significance of redox processes in these organisms. For instance, plants are among those organisms that suffer the most from the damaging actions of SO_2. However, different members of the plant kingdom manifest different levels of sensitivity to the gas. Among trees, the most sensitive are fir and pine, whereas the least sensitive are birch and oak. The highest sensitivity to SO_2 among flowering plants is attributed to the rose.

In humans, inhalation of air containing more than 0.2% of sulfurous gas causes shortness of breath and confusion. Prolonged and repeated exposure to SO_2 leads to loss of appetite, constipation, and inflammatory diseases of the respiratory tract. The levels of sensitivity to the gas differ from individual to individual. Sensitivity usually diminishes with prolonged exposure. This is explained by the induction of cytochrome protective activity that allows for a normal electron transport (up to a certain time); see Prousek (1988). It is likely that the reductive properties of dithionites (salts of dithionous acid $H_2S_2O_4$) are partially explained by $S_2O_4^{2-} = 2SO_2^{-\bullet}$, a dithionite reversible dissociation. Both dithionite ion and sulfur dioxide anion-radical can act as reducers. The former can be oxidized into sulfite or sulfate; the latter can lose an electron, thus transforming into a volatile dioxide (SO_2). This is why the use of a stable sodium dithionite during dye vatting or dye printing is always complicated with sulfurous gas evolution.

Dissociation of the dithionite ion can proceed both in aqueous and in nonaqueous media. There is a special equation to determine the average values of equilibrium constants (K_{eq}) of the formation of $SO_2^{-\bullet}$ from $S_2O_4^{2-}$ (Lough and McDonald 1987), namely, $K_{eq} = [SO_2^{-\bullet}]^2/\{[S_2O_4^{2-}]_0 - 0.5[SO_2^{-\bullet}]\}$. In DMF, DMSO, and AN, the K_{eq} values are 42.4, 11.3, and 40 mM at 25°C, respectively. These values exceed K_{eq} in water (1.4×10^{-6} mM) by 7 orders of magnitude.

Salt $(Et_4N)_2S_2O_4$ is very soluble in water and organic solvents. In nonaqueous media, its dissociation strongly depends on the moisture content. With the increase of water content from 0 to 20 vol.% in DMF, K_{eq} values fall from 42.4 to approximately 10^{-4} mM. Dithionite ions ($S_2O_4^{2-}$) are better stabilized in organic solvents of high polarity and in water (the polar solvent too) than in systems of low polarity (Lough and McDonald 1987).

Polar organic solvents are typical for electron-transfer reactions in organic chemistry. Although nonpolar organic solvents are not good at stabilization of $SO_2^{-\bullet}$, it is easily formed in such solvents also. Since organic reactants consume this anion-radical just after its formation, the problem of stabilization in bulk becomes unessential. Consequently, usage of $SO_2^{-\bullet}$ allows widening a range of solvents acceptable for organic electron transfer reactions. This makes $SO_2^{-\bullet}$ to be a particularly interesting one-electron donor.

1.7.7 Sulfite Radical

The $(SO_3)^{-\bullet}$ radical is essentially the sulfur trioxide anion-radical. It is named the sulfite anion-radical because it is obtained from sodium sulfite on reaction with titanium trichloride in water. This reaction usually proceeds in the presence of ethylene diamine tetraacetic acid as a complexing agent and hydrogen peroxide as an oxidant (Bradic and Wilkins 1984). Under these conditions, the

formation of $SO_3^{-\bullet}$ results from oxidation of SO_3^{2-} by $^\bullet OH$ radical: $Ti^{3+} + H_2O_2 \rightarrow Ti^{4+} + {}^\bullet OH + {}^-OH$, then $^\bullet OH + SO_3^{2-} \rightarrow {}^-OH + SO_3^{-\bullet}$. As seen, the formation and further reactions of $SO_3^{-\bullet}$ take place in alkaline medium. Therefore, there are some restrictions to the electron-transfer reactions from this anion-radical to acceptors. For instance, aliphatic nitro compounds react in alkaline mediums in aciforms. They add $SO_3^{-\bullet}$ to give new anion-radicals: $RCH{=}NOO^- + SO_3^{-\bullet} \rightarrow RCH(SO_3)NO_2^{-\bullet}$ (Bradic and Wilkins 1984).

To generate $SO_3^{-\bullet}$ in acidic mediums, the reaction between sodium hydrogen sulfite and cerium ammonium nitrate should be employed. In $(NH_4)_2Ce(NO_3)_6$, cerium has 4+ oxidation state. In acidic mediums, $(NH_4)_2Ce^{4+}(NO_3)_6$ easily oxidates the sulfite ion: $Ce^{4+} + SO_3^{2-} \rightarrow Ce^{3+} + SO_3^{-\bullet}$. This method of $SO_3^{-\bullet}$ generation is used to perform the addition of the sulfite anion-radical to unsaturated compounds: $RCH{=}CHR + SO_3^{-\bullet} \rightarrow RCH(SO_3^-)CH^\bullet R$.

This addition reaction is also applicable to substrates containing C≡C and C=S bonds (Ozawa and Kwan 1985). In cases of nonsymmetrically substituted double bonds, the less-shaded carbon atom is attacked by $SO_3^{-\bullet}$ anion-radical. For example, acrylic, dimethyl acrylic, and crotonic acids react with $SO_3^{-\bullet}$ at the expense of that ethylenic carbon, which is remote from the carboxylic group. Because these unsaturated acids are stable in alkali medium, it was possible to examine their anionic forms in the reaction with $SO_3^{-\bullet}$. As it turned out, the carboxylate group prevents $SO_3^{-\bullet}$ from entering the geminal position. At the same time, a competition is possible in alkaline medium for an unsaturated substrate between radicals $SO_3^{-\bullet}$ and $^\bullet OH$. The initial reaction between hydrogen peroxide and titanium (4+) is the source of the hydroxyl radical. The preceding restrictions for $SO_3^{-\bullet}$ addition are not relevant to $^\bullet OH$ addition. In contrast to anion-radical $SO_3^{-\bullet}$, radical $^\bullet OH$ bears no charge. Therefore, there is no electrostatic repulsion between the entering reactant (the hydroxy radical) and the substrate carboxylate group.

Depending on the structure of ethylenic compounds, addition of $SO_3^{-\bullet}$ to C=C bonds can be performed both in alkaline and in acidic solution. In acidic mediums, the addition proceeds easier than in the alkaline ones (Ozawa and Kwan 1985).

The reactions of $SO_3^{-\bullet}$ anion-radicals with organic and inorganic compounds have commanded considerable interest because of the role of these anion-radicals in grievous health and technological problems. Indeed, biochemical and industrial sources produce SO_3^{2-}. SO_3^{2-} is often transformed into $SO_3^{-\bullet}$ during atmospheric reactions. Both of them are pollutants whose activity in the environment leads to ailments (Reed et al. 1986).

1.7.8 Sulfate Radical

The $(SO_4)^{-\bullet}$ radical is essentially the sulfur tetroxide anion-radical. It is named the sulfate radical because it is formed from the persulfate ion as a result of UV irradiation or heating (at 80–100°C) of persulfate salts $M_2S_2O_8$ in aqueous solutions. Under these conditions, $S_2O_8^{2-} \rightarrow 2SO_4^{-\bullet}$ dissociation takes place (Minisci et al. 1983, Dias and Vieira 1996).

Conventional oxidants can, in principle, accept electrons from persulfate ions to form the sulfate anion-radical, but the reaction is extremely slow. For instance, $M_2S_2O_8$ in H_2O_2 solution gives M_2SO_4 for 2 months at 0°C (Skogareva and Ippolitov 1988). The presence of transition metal salts (e.g., salts of Ag^+ or Tl^{3+}) promotes the reaction (Minisci et al. 1983). In this case, each $S_2O_8^{2-}$ anion generates only one $SO_4^{-\bullet}$ anion-radical according to the following equation:

$$S_2O_8^{2-} + Ti^{3+} \rightarrow Ti^{4+} + SO_4^{2-} + SO_4^{-\bullet}$$

The transition metal nature is not essential for this redox reaction. However, one of the reaction products, namely, the anion-radical $SO_4^{-\bullet}$, can be complexed by a transition metal in a higher oxidation state. This leads to some stabilization of $SO_4^{-\bullet}$ and increases its reactive concentration. In other words, further reactions with organic substrates are facilitated (Fristad and Peterson 1984).

Cuprous and ferrous salts are preferable. Sometimes, a transition metal salt is deliberately added to a mixture of a substrate and a persulfate salt (Dobson et al. 1986). The free or metal-coordinated sulfate anion-radical reacts with an organic substrate, giving rise to a substrate cation-radical (Minisci et al. 1983, Itahara et al. 1988, Telo and Vieira 1997). The substrate cation-radical is often able to expel a proton and transform into the corresponding radical. The latter regenerates the initial metallic ion. The whole reaction becomes a catalytic one with respect to the metal.

$$RCH_3 + SO_4^{-\bullet} \rightarrow SO_4^{2-} + (RCH_3)^{+\bullet}$$

$$(RCH_3)^{+\bullet} \rightarrow H^+ + RCH_2^{\bullet}$$

$$RCH_2^{\bullet} + Cu^{2+} \rightarrow Cu^+ + RCH_2^+$$

$$RCH_2^+ + H_2O \rightarrow H^+ + RCH_2OH$$

In aqueous *tert*-butanol, pulse radiolysis of potassium persulfate and *p*-nitrobenzaldehyde induced consecutive reactions with the eventual formation of the *p*-formylphenoxyl radical (Geeta et al. 2004):

$$p\text{-}NO_2\text{–}C_6H_4\text{–}CH{=}O + SO_4^{-\bullet} \rightarrow SO_4^{2-} + (p\text{-}NO_2\text{–}C_6H_4\text{–}CH{=}O)^{+\bullet}$$

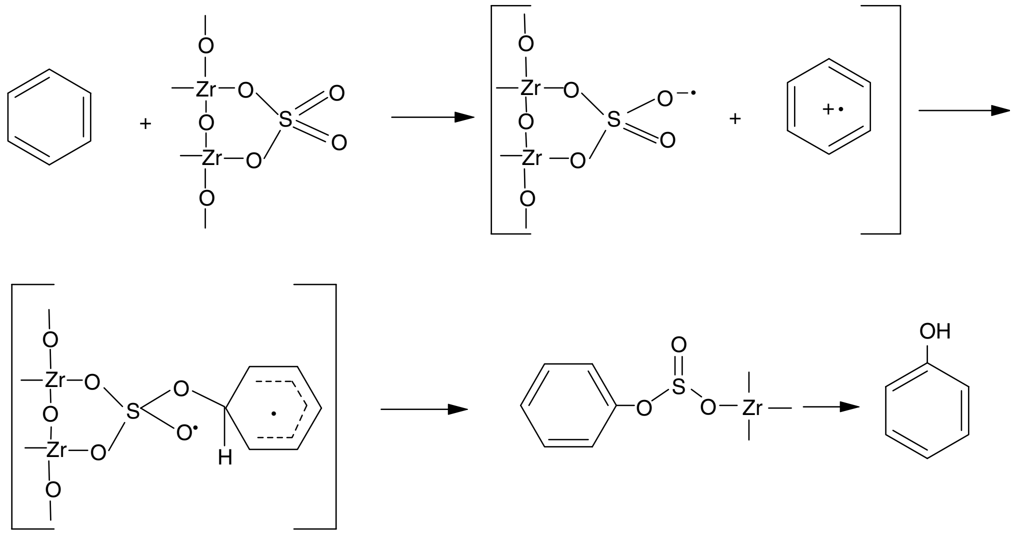
$$(p\text{-}NO_2\text{–}C_6H_4\text{–}CH{=}O)^{+\bullet} + H_2O \rightarrow HNO_2 + O{=}CH\text{–}C_6H_4\text{–}O^{\bullet}$$

Let us direct our attention to the difference between the anion-radicals $SO_4^{-\bullet}$ and $CO_2^{-\bullet}$. While the latter is a one-electron reductant (see section 1.7.4), the former is a one-electron oxidant. One-electron transfer from a substrate to the sulfate radical mostly follows diffusion rates. For instance, rate constants of one-electron oxidation of benzene and anisole with $SO_4^{-\bullet}$ are equal to 3×10^9 and 5×10^9 L mol^{-1} s^{-1}, respectively (Goldstein and McNelis 1984).

The sulfate anion-radical is not a very strong hydrogen acceptor. It acquires the atomic hydrogen from organic substrates at significantly smaller rates as compared with the rates of one-electron oxidations. For instance, dehydration rate constants are 10^7, 10^6, and 10^5 L mol^{-1} s^{-1} for methanol, *tert*-butanol, and acetic acid, respectively (Goldstein and McNelis 1984, Zapol'skikh et al. 2001). Such a peculiarity is very important for the selectivity of ion-radical syntheses with the participation of $SO_4^{-\bullet}$.

If the sulfate anion-radical is bound to the surface of a catalyst (sulfated zirconia), it is capable of generating the cation-radicals of benzene and toluene (Timoshok et al. 1996). Conversion of benzene on sulfated zirconia was narrowly studied in a batch reactor under mild conditions (100°C, 30 min contact) (Farcasiu et al. 1996, Ghenciu and Farcasiu 1996a, 1996b). The proven mechanism consists of a one-electron transfer from benzene to the catalyst, with the formation of the benzene cation-radical and the sulfate radical on the catalytic surface. This ion-radical pair combines to give a surface combination of sulfite phenyl ester with reduced sulfated zirconia. The ester eventually gives rise to phenol (Scheme 1.45). Coking is not essential for the reaction shown in Scheme 1.45. Oxidation completely resumes the activity of the worked-out catalyst.

Reactions of the sulfate radical characterize it as a strong oxidant ($E^0 \approx 2.60$ V, in water—Balej 1984). Like organic anion-radicals, $SO_4^{-\bullet}$ has some affinity to hydrogen radical. With cyclic alkynes, the sulfate anion-radical acts as an oxygen-transfer reagent, transforming the alkyns in α,β-epoxy compounds (Wille 2000). In this sense, the sulfate radical can also be considered as a donor of atomic oxygen in solution. The reaction leads to the release of $SO_3^{-\bullet}$, which is significantly less reactive than $SO_4^{-\bullet}$ (Muller et al. 1997). In contrast to organic anion-radicals, $SO_4^{-\bullet}$ possesses



SCHEME 1.45

high electrophilicity and is prone to additional reactions (Davies and Gilbert 1985a). Some examples are as follows:

$$CH_2{=}CHCH_2OH + SO_4^{-\bullet} \rightarrow {}^{-}O_3SOCH_2CHCH_2OH$$

$$MeCH{=}CHCOOH + SO_4^{-\bullet} \rightarrow MeCHCH(OSO_3^{-})COOH$$

$$CH_2{=}CHCH_2COOH + SO_4^{-\bullet} \rightarrow {}^{-}O_3SOCH_2CH^{\bullet}CH_2COOH$$

The reactions enumerated lead to the adducts that are observable by means of the ESR method. In the cases of maleic and fumaric acids, ESR spectra can be recorded at high enough pH values only: Being a strong electrophile, radical $SO_4^{-\bullet}$ is more active toward a carboxylate ion than to neutral molecules of unsaturated acids.

Carboxylate ions of saturated acids react with the sulfate radicals, giving rise to carboradicals (Eberson et al. 1968):

$$Me_3CCOO^{-} + SO_4^{-\bullet} \rightarrow SO_4^{2-} + Me_3CCOO^{\bullet}$$

$$Me_3COO^{\bullet} \rightarrow CO_2 + Me_3C^{\bullet}$$

This reaction resembles decarboxylation of carboxylates during electrode one-electron oxidation (Kolbe reaction). Kolbe reaction also consists of one-electron oxidation, decarboxylation, and culminates in dimerization of alkyl radicals just after their formation at the electrode surface. When the sulfate radical acts as a one-electron oxidant, the caboradical dimerization is hampered. The radicals can be used in preparative procedures. One typical example is alkylation of heterocyclic nitrogen bases (Minisci et al. 1983). This difference between Kolbe reaction and the reaction with the help of a "dissolved" electrode (the sulfate radical) deserves some explanation. The concentration of the one-electron oxidation products in the electrode vicinity is significantly higher than that in the bulk of the solution. Therefore, in the case of anode-impelled reactions, the dimerization of radicals produced from carboxylates proceeds easily. Noticeably, $SO_4^{-\bullet}$ secures the single electron nature of oxidation more strictly than an anode. In electrode reactions, radical intermediates can

undergo further oxidation if potentials of capturing the first and the second electrons are more or less close. In contrast, the homogeneous reactions with the participation of $SO_4^{-\bullet}$ are characterized by fixed potentials with respect to the reactant and an organic substrate. The route of homogeneous reactions strongly depends on the ratio of reagent concentrations. If the ratio is small, the probability of the secondary reaction is low. The distinction can be illustrated with the oxidation of $RCOO^-$: It can give $R^\bullet$ and after that, at once, R^+ in an anodic process. In the case of oxidation with the aid of $SO_4^{-\bullet}$, $R^\bullet$ becomes the sole product of the reaction (Eberson et al. 1968).

Another advantage of the $SO_4^{-\bullet}$ pathway for carboradical generation is its high selectivity. As noted earlier, this type of oxidation allows one to avoid (practically) the hydrogen abstraction. In the case of alkyl carboxylates, the rate of one-electron oxidation of the carboxyl group exceeds the rate of homolytic disruption of the C—H bond in an alkyl rest by 100 times (Davies et al. 1985a,b). Cleavage of persulfate in the presence of carboxylates is a simple and reliable method of getting alkyl radical for synthesis.

1.7.9 Hydroxide Anion

This anion is a typical reagent for organic hydroxylation. Many such reactions have ion-radical mechanisms according to which an inorganic anion transfers an electron to an organic substrate. It is important to underline the diffuse nature of an electron of the lone pair on the ^-OH ion, which allows MOs of the ion and the substrate to overlap despite a long enough distance between them (Takahashi et al. 2001). For example, in the reaction between the hydroxyl anion and *o*-dinitrobenzene, ^-OH ion is proved to be an electron donor (see Section 4.3.4.2). The result consists of ^-OH transformation into $^\bullet OH$ and *o*-dinitrobenzene into the anion-radical. The *o*-dinitrobenzene anion-radicals are stable. The anion-radicals come into the reaction volume and combine with new hydroxide ions (Abe and Ikegame 1978).

$$C_6H_4(NO_2)_2 + {}^-OH \rightarrow {}^\bullet OH + C_6H_4(NO_2)_2^{-\bullet}$$

$$C_6H_4(NO_2)_2^{-\bullet} + {}^-OH \rightarrow {}^-C_6H_4(NO_2)(OH)NO_2^-$$

$${}^-C_6H_4(NO_2)(OH)NO_2^{-\bullet} + C_6H_4(NO_2)_2 \rightarrow C_6H_4(NO_2)_2^{-\bullet} + {}^-C_6H_4(NO_2)(OH)NO_2$$

$${}^-C_6H_4(NO_2)(OH)NO_2 \rightarrow NO_2^- + C_6H_4(OH)NO_2$$

There are several cases of hydroxylation according to the "hidden-radical" mechanism, within a solvent cage. As assumed (Fomin and Skuratova 1978), hydroxylation of the anthraquinone sulfonic acids (AQ—SO_3H) proceeds by such a reticent pathway, and $^\bullet OH$ radicals attack the substrate anion-radicals in the solvent cage. Anthraquinone hydroxyl derivatives are the final products of the reaction. In the specific case of DMSO as a solvent, hydroxyl radicals give complexes with the solvent and lose their ability to react with the anthraquinone sulfonic acid anion-radicals (Bil'kis and Shein 1975). The reaction stops after an anion-radical is formed:

$$AQ{-}SO_3^- + {}^-OH \rightarrow {}^\bullet OH + (AQ{-}SO_3^-)^{-\bullet}$$

$$Me_2SO + {}^\bullet OH \rightarrow Me_2SO^\bullet OH \rightarrow Me^\bullet + HOSOMe$$

The hidden-radical mechanism (also dubbed "the mechanism of biradical origin") does not, however, take into account all the peculiarities of the reaction participants. The redox potential of $^-OH/^\bullet OH$ couple is equal to 0.9 V with regard to the saturated calomel electrode in AN (Tsang et al. 1987). In conventional reference to the normal hydrogen electrode and in water, this potential is equal to 1.9 (Berdnikov and Bazhin 1970) or 1.3 V in AN (Eberson 1987, Chapter 4, p. 62).

These values are not appropriate for reducing the majority of the organic acceptors. Of course, there are some cases of single electron transfer from ^{-}OH ion to an organic acceptor. All these cases, however, refer to substrates with very strong electron affinity, such as tetracyanoethylene or dinitrobenzene (Blumenfel'd et al. 1970). Quinones, ketones, and other substrates have less affinity. In the ground (unexcited) states, they are unable to capture an electron from the ^{-}OH ion (Sawyer and Roberts 1988).

The described reactions of quinone hydroxylation as well as electron transfer from hydroxide ion to quinones are, in general, accelerated by light irradiation. Wavelengths are up to 500 nm. The degree of acceleration is higher with greater intensity of irradiation and with an increase in the concentrations of quinone and hydroxide (Blumenfel'd et al. 1970). Direct (outer-sphere) electron transfer takes place from hydroxide to an excited quinone molecule. In the excited molecule, one of the electrons of a double-occupied orbital populates a vacant orbital. The "derelict" orbital is located at a lower energy level than that of the vacant orbital. Therefore, the electron transfer from hydroxide to a quinone becomes energetically favorable. This corresponds to an enhanced electron affinity and lifts the prohibition of the electron transfer.

It should be pointed out that the possibility of an $^{-}OH \rightarrow {}^{\bullet}OH$ transformation with one-electron transfer to a substrate depends on the fate of the resulting hydroxyl radical. The latter is a strong oxidant and it must be removed from the reaction sphere to shift the electron-transfer equilibrium to the right. One way to shift the equlibrium to the right is the recombination of two $^{\bullet}OH$ radicals, which results in H_2O_2 formation. As a rule, hydrogen peroxide is formed by reactions between hydroxide and very strong acceptors (Endo et al. 1984). However, an attack of the hydroxyl anion on an unsaturated site of a substrate (an aromatic fragment, a carbonyl group, etc.) is chemically very typical and interesting. This results in a σ- complex formation. Such a complex can regroup into a product of hydroxylation. The complex can also decay with the formation of substrate anion-radicals and $^{\bullet}OH$ radicals. In brief, the electron transfer proceeds in an inner-sphere manner, and the aforementioned restrictions (in potential differences, in $^{\bullet}OH$ oxidation activity) vanish. This inner-sphere mechanism is assumed to be the most frequent. Finally, there are two rare extremes, namely, the straightforward ion-radical mechanism and the mechanism including the formation of σ complexes (e.g., Meisenheimer or Yanovsky complexes).

The last but not the least peculiarity of the reaction between ^{-}OH and electron acceptors is its dependence on solvation effects. Solvation energy affects the ionization potential of ^{-}OH and an electron affinity of a substrate as well. For instance, the ^{-}OH ion is a stronger base and a more effective electron donor in AN or DMSO than in water. Its solvation energy is lower by 80–100 kJ mol^{-1} in these organic solvents than in water (Sawyer and Roberts 1988). This fall in the solvation energy corresponds to a relief of hydroxyl anion oxidation by almost 1 V (Sawyer and Roberts 1988). As for the other participants in the equilibrium reaction of electron transfer (a neutral substrate, its anion-radical, and the $^{\bullet}OH$ radical), their solvation susceptibility is not so essential. The main effect should be attributed to ^{-}OH. However, the ability of ^{-}OH to be an electron donor depends not only on its solvation energy, but also on the energy of covalent binding of the hydroxyl group to an adduct with a substrate or on the total energy of a final product of hydroxylation.

1.7.10 Nitrosonium and Nitronium Ions

The nitrosonium ion, ^{+}NO, is a strong oxidant with E^0 = 1.51 V versus the normal hydrogen electrode. It reacts with organic substrates with E^0 < 1.7 V as an outer-sphere acceptor of one electron. In contrast, the nitronium ion, NO_2^{+}, is a weaker oxidant than the nitrosonium ion, although its redox potential (E^0 = 1.56 V versus the normal hydrogen electrode) is very close to that of the nitrosonium ion. The sharp decrease in acceptor properties is due to the energy consumption that is necessary to change the NO_2^{+} structure on one-electron transfer. The $(O{=}N{=}O)^{+} \rightarrow (O{::}N{::}O)^{\bullet}$ transformation leads to some lengthening of the N–O bond that requires an external energy of 42 kJ mol^{-1}. If this transformation proceeds in a solution, the solvent reorganization energy

does not exceed 105 kJ mol^{-1} (Eberson and Radner 1987). Meanwhile, $(O{=}N{=}O)^+$ ion is linear and $(O{::}N{::}O)^\bullet$ radical is bent (O—N—O angle is equal to 134.3°). The bending consumes considerable energy, estimated to be 218 kJ mol^{-1} (Eberson and Radner 1987) or even 587 kJ mol^{-1} (Lund and Eberson 1997). The bond reorganization energy is the main factor that decreases the NO_2^+ electron affinity. Only highly oxidizable substrates can participate in the outer-sphere electron transfer to NO_2^+. The observed cases of generating substrate cation-radicals and the nitrogen dioxide radicals are stipulated by the inner-sphere mechanism. Such a mechanism involves the attack of the nitronium ion on a substrate, formation of a tetrahedral complex, and disintegration of the complex. The disintegration results in products, which formally corresponds to a one-electron transfer. However, the reorganization energy is lower for the inner-sphere mechanism since the bending of the nitronium ion is no longer required.

Thus, there is a great difference in electron-transfer reactivity between the nitronium and the nitrosonium ions, despite their redox potentials being close. Closeness in the electrode potentials supposedly reflects the peculiarities of electrochemical reactions. The liquid-phase reactions discussed here have their own string of distinctions. Electrode processes are heterogeneous. There is a strong electric field in the near-electrode layer. The field can have an effect on the behavior of the NO_2^+ ion. It is probable, under the electrode reaction conditions, that both the linear NO_2^+ and the bent $NO_2^\bullet$ radicals acquire somewhat similar configuration in the tough part of the double electric layer. Energy consumption for such a small bend is revealed in the potential value only vaguely (cf. 1.56 and 1.51 V for the couples of $NO_2^\bullet/NO_2^+$ and $NO^\bullet/NO^+$, respectively). Some authors suggest that the experimental values determined for $NO_2^\bullet/NO_2^+$ might be influenced by significant orbital overlap between $NO_2^\bullet$ and the Pt electrode surface (Lee et al. 1991). The pathway is energetically favored because the outer-sphere reorganization energy is not needed as much. Of course, a solvent can intervene in all of these phenomena. It should be noted that $E^0(NO_2^\bullet/NO_2^+)$ in AN has been reported to be over 0.6 V less than $E^0(NO_2^\bullet/NO_2^+)$ in sulfolane and nitromethane (Boughriet and Wartel 1989a, 1989b, 1993).

In homogeneous liquid-phase reactions, there are no strong electric fields and no influence of a tough electrode layer. Geometric factors begin to play their independent roles. These factors determine the equilibrium state, which governs the degree of conversion of the acceptor (NO_2^+, NO^+) during one-electron transfers. Moreover, the NO_2^+ ion can form a complex with a solvent (Ciaccio and Marcus 1962, Hunziker et al. 1971). This causes a marked diminution of the NO_2^+ reactivity and decreases the nitration rates. The NO_2^+ and NO^+ reactivity problem is also considered with respect to aromatic nitration (see Section 4.5.4).

It is natural that the participation of NO_2^+ and NO^+ in the one-electron oxidation puts forward the target of $NO_2^\bullet$ and $NO^\bullet$ determination. The direct determination of these gaseous products presents some problems. IR spectroscopy is a method (see, e.g., Todres et al. 1988), but this method is not always convenient or even available. The direct determination of $NO_2^\bullet$ and $NO^\bullet$ by ESR spectroscopy is not possible owing to the short relaxation time, which gives rise to broad absorption lines. Spin trapping of $NO^\bullet$ combined with ESR is recommended for this purpose (Norby et al. 1997). As an effective spin trap for $NO_2^\bullet$, poly(2-vinylpyridine) has been recently proposed (Davydov et al. 2006).

1.7.11 Tris(aryl)amine and Thianthrene Cation-Radicals

In 1966, Walter had developed the preparation and studied redox properties of tris(aryl)amine cation-radicals. Then these cation-radicals have found wide applications in organic synthesis. For example, salts of the tris(4-bromophenyl)amine and tris(2,4-dibromophenyl)amine cation-radicals (occasionally named "Magic Blue" and "Magic Green") with the hexachloroantimonium anion are stable and frequently used for the initiation of diverse reactions that begin with the cation-radical formation. The nature and reactivity of inorganic counterions control the stability and redox properties of these organic cation-radicals. The aspects mentioned are analyzed here. Generation of the

tris(bromophenyl)amine cation-radical takes place when the tris(bromophenyl)amine is oxidized with antimony pentachloride according to the following equation:

$$2(4\text{-}BrC_6H_4)_3N + 3SbCl_5 \rightarrow SbCl_3 + 2(4\text{-}BrC_6H_4)_3N^{+\bullet}SbCl_6^-$$

Formation of the $SbCl_6^-$ anion is a result of the following disproportionation:

$$2SbCl_5 \rightarrow SbCl_6^- + SbCl_4^+$$

$$SbCl_4^+ + (4\text{-}BrC_6H_4)_3N \rightarrow (4\text{-}BrC_6H_4)_3N^{+\bullet} + SbCl_4^{\bullet}$$

$$2SbCl_4^{\bullet} \rightarrow SbCl_5 + SbCl_3$$

Anion $SbCl_6^-$ is a good oxidizing agent because it can be reduced from Sb^V to Sb^{III}. Organic substrates with E^0 up to 1.5 V versus the normal hydrogen electrode transform into cation-radicals in the presence of $SbCl_6^-$. Note: Tris(4-bromophenyl)amine has $E^0 = 1.3$ V versus the normal hydrogen electrode in AN (Reinolds et al. 1974). Such an acceptor influence of the anion in the salt provides high stability to the salt. In cases of other anions, the cation-radical component decays gradually (both as a dry solid and in a solution) (Eberson and Larsson 1986). The main role in such a degradation belongs to the reaction between the cation-radical and water (from air or as a solvent moisture). Cation-radicals of tris(aryl)amines can decompose water at room temperature. The reaction resembles the process of water decomposition with oxidized forms of chlorophyll *a* and consists of the formation of hydrogen peroxide. The peroxide is the source of oxygen (Pokhodenko et al. 1984):

$$Ar_3N^{+\bullet} + H_2O \rightarrow Ar_3N + H^+ + ½H_2O_2$$

$$H_2O_2 \rightarrow H_2O + ½O_2$$

The oxygen and hydrogen peroxide evolving in the reaction provoke the degradation of tris(4-bromophenyl)amine. Another route of degradation consists of the gradual dimerization of these cation-radicals with bromine depletion (Cowell et al. 1970). However, having the hexachloroantimonate counterion, tris(4-bromophenyl)ammoniumyl is stable (Pokhodenko et al. 1984, Cowell et al. 1970). According to International Union of Pure and Applied Chemistry (IUPAC) rules, ammoniumyl is the name for amine cation-radicals.

Like all cation-radicals, ammoniumyls are sensitive to nucleophiles (as reactants or as admixtures). At the same time, 1,1,1,3,3,3-hexafluoropropan-2-ol as a solvent drastically curtails nucleophilic reactivity and provides good integrity of tris(4-bromophenyl) ammoniumyl at ambient temperatures (Eberson et al. 1996).

In cases when tris(4-bromophenyl)ammoniumyl hexachloroantimonate turns out to be weak as a one-electron oxidant, its 2,4-dibromo- or even 2,3,4,5,6-hexachloro-analog is employed (Nelsen et al. 1997). After one-electron oxidation, these ammoniumyls transform into tris(aryl)amines, and hexachloroantimonate begins to serve as a counterion for newly formed cation-radicals of a donor substrate. It should be noted that tris(aryl)amines are remarkably nonreactive as nucleophiles. Hexachloroantimonate possesses not very strong, but appreciable nucleophilicity. One can use ammoniumyl hexabromocarboranes: This change brings the anion's nucleophilicity to zero.

Stepwise oxidation of organic substrates is often carried out with thainthreniumyl perchlorate. This oxidant will be encountered in many cases during the citing of materials in the following chapters. However, first, a safety warning should be put. It is a shock-sensitive solid that must be handled only on a small scale and with due care.

1.7.12 Trialkyloxonium Hexachloroantimonates

These salts belong to a widely used class of alkylating agents; their traditional name is Meerwein's salts (Meerwein et al. 1937). However, they can be involved in reactions other than alkylation (Boettger et al. 1997). One of these reactions is the oxidation of aromatic donors (Rathore et al. 1998a, Rathore and Burns 2003):

$$2ArH + 3(Et_3O^+SbCl_6^-) \rightarrow 2(ArH^{+\bullet}SbCl_6^-) + 3EtCl + 3Et_2O + SbCl_3$$

The triethyloxonium cation is an effective oxidant for the production of aromatic cation-radicals, but only as the hexachloroantimonate salt. The analogous $Et_3O^+BF_4^-$ or $Bu_4N^+SbCl_6^-$ cannot be used to prepare any cation-radical. This is consistent with the previously described function of $SbCl_6^-$ as an oxidant. The slow release of $SbCl_5$ forms the basis for the efficacy of $Et_3O^+SbCl_6^-$. Kochi's group describes this slow release as follows (Rathore et al. 1998a):

$$Et_3O^+SbCl_6^- \rightarrow SbCl_5 + EtCl + Et_2O$$

The transformations of $SbCl_5$ caused by a one-electron transfer from an aromatic compound have been described earlier. If the pure Lewis acid $SbCl_5$ is used, its reactivity is very difficult to control, and single-electron oxidation as well as chlorination of various aromatic donors can occur readily (Mori et al. 1998). Meanwhile, in the case of $Et_3O^+SbCl_6^-$, the slow release of the active monomer $SbCl_5$ occurs. In the case of $SbCl_5$ as such, the $2SbCl_5 \rightarrow Cl_4Sb\text{—}Cl_2\text{—}SbCl_4$ dimerization occurs (Cotton and Wilkinson 1988, p. 395). The dimeric form may lead to the following electrophilic chlorination:

$$SbCl_4\text{—}Cl_2\text{—}SbCl_4 + 2ArH \rightarrow 2ArCl + 2HCl + SbCl_3$$

Neither Et_3O^+ nor $SbCl_6^-$ is individually capable of aromatic oxidation. Therefore, the slow-released monomeric $SbCl_5$ is the active oxidant. This is a reason to consider trialkyloxonium hexachloroantimonates together with other inorganic participants of organic ion-radical reactions.

1.7.13 Transition Metal Ions

In terms of electron transfer reactions, transition metal ions can be the one- or two-electron type. The two-electron ions transform into unstable states on unit change of the metal oxidation number. In the outer-sphere mechanism, two-electron transfer is a combination of two one-electron steps.

The conditions of the outer-sphere mechanism have been analyzed at length in literature (Eberson 1987, Chapter 7). An organic substrate must fit a metal ion with respect to redox potentials. The substrate cannot have any hydrogen atom that is prone to depart as a proton. The substrate cannot have any positions that are free from any steric stoppage for a metal attack. The metal ion has to have a relatively high redox potential, and this potential has to be away by no less than 0.5 V from potentials of the next redox transformations of the ion. Ligands surrounding the metal ion cannot be substituted with the substrate in electron-transfer reactions. Otherwise, the reaction system is directed to the route of inner-sphere electron transfer. The same concern has to do with ligand exchange at the expense of medium components. Participation of a transition metal ion in electron transfer leads, of course, to some changes in redox properties. For the outer-sphere mechanism, it is important that the change of the redox potential would not affect the reorganization energy of solvate environment of the metallic ion. It is better to restrict the metal ion-substrate interaction sterically at both the metal and substrate sides.

In all other cases, inner-sphere mechanisms are at work. These mechanisms include addition and subsequent dissociation. For C—H dissociation, the so-called metallocomplex activation

takes place. This kind of activation consists of inner-sphere electron transfer as it is exemplified with the following equation:

$$R^{\bullet} + Cu^{II}(OAc)_2 \rightarrow RCu^{III}(OAc)_2 \rightarrow R(-H^{\bullet}) + HOAc + Cu^{I}OAc$$

One example of outer-sphere electron transfer is the reaction between the dipotassium cyclooctatetraene ($K_2C_8H_8$) and the cobalt complex of bis(salicylidenediamine) (Co^{II}Salen) (Levitin et al. 1971).

$$K_2C_8H_8 + 2Co^{II}Salen \rightarrow C_8H_8 + 2(Co^{I}Salen)^{-}K^{+}$$

Although $C_8H_8K_2$ is a two-electron donor, only a one-electron transfer takes place. Only this type of transfer is permitted due to the difference between the potentials of the donor and the acceptor. This difference remains a determining factor of electron exchange because the cobalt atom firmly reserves the ligand environment for itself. As for cyclooctatetraene, it is unable to provide the ligand exchange in this case. The results obtained helped in solving the inverse problem, namely, development of an analytical method for determination of $Co^{0}Salen^{2-}$. This deeply reduced dianionic form of the complex results in the metallic sodium reduction of Co^{II}Salen. The dianionic form possesses catalytic properties and is actively used in model studies of biological electron transport. After the treatment of Co^{II}Salen with excess sodium in THF, the reduced product was allowed to react with cyclooctatetraene; the consumption of cyclooctatetraene quantitatively was determined by means of gas–liquid chromatography. If an insufficient amount of C_8H_8 was used, C_8H_8 was transformed into $C_8H_8Na_2$ completely. If the amount of C_8H_8 employed was 1 mol per 2 mole of Co^{II}Salen used to obtain $[(Co^{0}Salen)^{2-}2Na^{+}]$, then the degree of transformation of C_8H_8 into $C_8H_8Na_2$ was 70%. This means that the “deeply reduced” sample contained only 70% of $[(Co^{0}Salen)^{2-}2Na^{+}]$. In that case, outer-sphere electron transfer looks like a “titration” of the double charged complex with cyclooctatetraene.

$$C_8H_8 + 2[(Co^{0}Salen)^{2-}2Na^{+}] \rightarrow C_8H_8Na_2 + 2[(Co^{I}Salen)^{-}\ Na^{+}]$$

Titration according to this scheme showed that the treatment of Co^{II}Salen with excess amounts of sodium resulted in nonquantitative formation of $[(Co^{0}Salen)^{2-}2Na^{+}]$. Thus, catalytic and, especially, kinetic investigations of such complexes have to take into account the presence of Co^{II}Salen or $(Co^{I}Salen)^{-}$ in the samples studied. The described convenient method of quantitative electron transfer in solutions is good at determining low-valence metallocomplexes.

The solvent role in electron-transfer reactions between organic substrates and metal ions is worth noting. For instance, transformation of Cu^{II} complex into a Cu^{I} complex proceeds better in AN than in water (Ahrland et al. 1983). Coordination of Cu^{I} with AN is much better than that with water. In water solutions, with no significant share of organic solvents, Cu^{I} salt disproportionates completely and yields Cu^{II} salts and Cu^{0} metal. In aprotic solvents, the Cu^{I} ion is much more stable. In DMSO, the disproportionation is not significant as long as the concentration of Cu^{I} is small. In pyridine, it does not proceed at all, irrespective of the concentration. In AN, Cu^{I} salts are absolutely stable with no signs of disproportionation or air oxidation. Thus, the role of an organic aprotic solvent consists of the enhancement of stability of a partly reduced form of metallocomplex or ion. The cause of such an enhancement is the more effective solvation than in the case of water or another proton donor solvent.

In connection to the data described earlier, one reasonable question arises: Why does the stabilizing role of a nonaqueous solvent become significant for Cu^{I} salts and remain insignificant for Cu^{II} salts? It was shown (Myagchenko et al. 1989) that Cu^{II} salts (and salts of Hg^{II} and Pd^{II} as well) exist in nonaqueous solutions as polynuclear compounds. Thus, $CuCl_2$ forms lamellar lattices with chlorine chains as bridges between copper atoms. In contrast, CuCl does not form such chain structures.

Cu^I ion is easily and effectively solvated by nonaqueous solvents and forms stable solvates. As far as $(CuCl_2)_n$ associates are concerned, their interactions with an organic solvent as well as with an organic substrate generally takes place at terminal groups, which are energetically active. Naturally, solvation of the associates, in which the metal ion is encapsulated, cannot be effective. The copper salts belong to the type of one-electron redox systems. Redox couples Co^{III}/Co^{II}, Co^{II}/Co^I, Mn^{III}/Mn^{II}, Ce^{IV}/Ce^{III}, Ag^{II}/Ag^I, Ir^{IV}/Ir^{III}, Fe^{III}/Fe^{II}, Cr^{III}/Cr^{II}, and W^{VI}/W^V also belong to the one-electron string.

The pair Tl^{II}/Tl^I is also used widely for one-electron oxidation in aqueous acidic solutions of organic substrate under pulse radiolysis. The aqueous solutions must be saturated with N_2O. The latter takes part in the reaction and the reaction leads to $HO^\bullet$ radical: $e_{aq} + NO_2 + H_2O \rightarrow N_2 + HO^\bullet + HO^-$. This $HO^\bullet$ radical generates the desired Tl^{II} from Tl^I: $HO^\bullet + Tl^I + H^+ \rightarrow Tl^{II} + H_2O$.

Being compared to ionic reactions, inorganic redox transformations usually proceed slowly. Therefore, sometimes, a more active couple needs to be selected. For instance, the one-electron reduction of aromatic diazocompounds by Fe^{II} (Fe^{III}/Fe^{II} couple) takes place sluggishly, whereas Ti^{III} (Ti^{IV}/Ti^{III} couple) reacts with the same substrates rapidly (Heinrich et al. 2006). Two-electron redox systems are represented by couples Tl^{III}/Tl^I, Pb^{IV}/Pb^{II}, Pd^{II}/Pd^0, Mg^{II}/Mg^0, Hg^{II}/Hg^0, Au^{III}/Au^I, Pt^{IV}/Pt^{II}, and Pt^{II}/Pt^0.

The action of one-electron redox systems is readily understandable in the context of inner- and outer-sphere mechanisms, whereas two-electron redox systems require additional considerations. First, if a double one-electron transfer is possible from an organic substrate to the same metal ion, does it mean that the same molecule of an organic donor provides these two electrons, or do two molecules of the substrate act as one-electron donors?

Oxidation of aromatic hydrocarbons with lead tetraacetate develops as the second-order reaction. Hence, the rate-determined stage consists of the transformation of Pb^{IV} to Pb^{II} with the participation of only one molecule of the hydrocarbon (Dessau et al. 1970). The formed hydrocarbon dication can, of course, react with the uncharged hydrocarbon: $ArH^{2+} + ArH \rightarrow ArH^{+\bullet} + ArH^{+\bullet}$.

The cation-radicals $ArH^{+\bullet}$ were detected, but they originated from the fast reaction of a one-electron transfer, which does not affect kinetic constants of the oxidation. The rate constant depends linearly on Brown's σ constants of substituents (Dessau et al. 1970). All these data are in agreement with the formation of the strong polar dication of an aromatic hydrocarbon as an intermediate. Because Pb^{II} salts (in particular the diacetate) are not reductants, the two-electron transfer reaction proceeds irreversibly.

In some cases, two-electron transfer to a metal ion leads to the formation of a reducing form. This gives a possibility to construct catalytic cycles. Oxidation of ethylene with Pd^{II} on catalysis of Cu^{II} is a striking example (Denisov 1978), that is,

$$CH_2{=}CH_2 + Pd^{II} \rightarrow (CH_2{=}CH_2) \cdot Pd^{II}$$

$$(CH_2{=}CH_2) \cdot Pd^{II} + H_2O \rightarrow Pd^0 + 2H^+ + CH_3CHO$$

$$Pd^0 + 2Cu^{II} \rightarrow Pd^{II} + 2Cu^I$$

$$Cu^I + O_2 \rightarrow Cu^{II} + O_2^{-\bullet} \quad Cu^I + O_2^{-\bullet} \rightarrow Cu^{II} + O_2^{2-}$$

$$O_2^{2-} + 2H^+ \rightarrow H_2O_2 \quad Cu^I + H_2O_2 \rightarrow 2OH^- + 2Cu^{II}$$

Sometimes, metal ion participation in electron transfer reactions can proceed with no changes in its oxidation state, simply at the expense of complex formations. The following equation illustrates such assistance by 3d metals ions (M = Mn, Co, Ni, and Zn) in electron transfer between a reductant (Red) and an oxidant (Ox): $M^{2+} + Red + Ox \rightarrow [Red–M^{2+}–Ox] \rightarrow Red^+ + M^{2+}(Ox^-)$.

A depth of this reaction correlates with the electron donor ability of Red and the stability degree of $M^{2+}(Ox^-)$ complex. The complexation causes anodic shift of metal redox potentials, which reaches almost 100 mV for transition metal cations (Maletin et al. 1979, 1980, 1983).

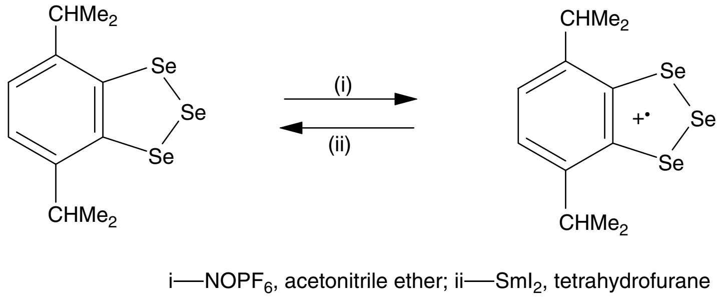
Alkali, alkaline-earth, and rare-earth metal cations also catalyze electron transfer reactions. Thus, in the pair of Co^{II}-tetraphenylporphyrin complex with BQ, no redox reaction takes place, or it takes place too slowly to be determined. The metal cations promote this reaction. For example, in the presence of $Sc(ClO_4)_3$, the corresponding rate constant of $2.7 \times 10^5\ M^{-2}\,s^{-1}$ was observed. BQ transforms into benzosemiquinone under these conditions (Fukuzumi and Ohkubo 2000). Zinc perchlorate accelerates the reaction between aromatic amines and quinones (Strizhakova et al. 1985). This reaction results in the formation of charge-transfer complexes $[ArNH_2^{\delta+} \cdots Q^{\delta-}]$. The complexes dissociate in polar solvents, giving ion-radicals:

$$ArNH_2 + Q \xrightarrow{K_1} [ArNH_2^{\delta+} \cdots Q^{\delta-}] \xrightarrow{K_2} ArNH_2^{+\bullet} + Q^{-\bullet}$$

Equilibrium constants K_1 and K_2 are low enough, and for the interaction of $ArNH_2$ with Q in AN at 20°C, $K_1 = 4.5 \times 10^{-2}$, $K_2 = 1.1 \times 10^{-6}$ (Levin et al. 1979). However, the addition of zinc ions sharply increases the rate of formation of the amine cation-radical, leaving the rate of formation of the quinone anion-radicals with no change. The influence of zinc ions on the electron transfer from an amine to a quinone can be explained by the binding of anion-radical $Q^{-\bullet}$ in a complex with Zn^{II}. This allows shifting the equilibrium to the right. However, the stability constant of another possible complex, $[Zn(ArNH_2)]^{2+}$, is equal to 10^5 and is much higher than K_1 (Strizhakova et al. 1985). In other words, introduction of Zn^{II} should produce the left, not the right, shift of the equilibrium. The complexation between $Q^{-\bullet}$ and Zn^{II} indeed takes place, but it does not preserve these anion-radicals from decaying in fast collateral reactions. Moreover, the anion-radical does not, before its decay, have enough time to leave the inner coordination sphere of the complex with zinc. This causes the shifting of the equilibrium to the right. Meanwhile, the observed result consists of an increase in the rate of accumulation of cation-radicals $ArNH_2^{+\bullet}$, but not that of anion-radicals $Q^{-\bullet}$.

Complexation between zinc ions and anion-radicals of aromatic ketones provides a basis for a simple method of one-electron ketone reduction (Handoo and Gadru 1986). In this method, DMSO is employed as a solvent, and zinc dust serves as a reductant in the presence of a strong alkali (6 M, several drops). As widely known, zinc in alkali medium is a very active reductant. For example, it reduces nitrates under such conditions to ammonia. In the ketone case, electron transfer is stopped at the stage of the ketyl formation. Proton donor treatment leads to the respective alcohols: benzophenone gives benzhydrol, fluorenone gives fluorenol, etc. Importantly, the ketones employed have electron affinity up to -210 kJ mol^{-1} (Handoo and Gadru 1986). All of them give anion-radicals with practically quantitative yields. A breakthrough feature of such a method of anion-radical generation is that it does not require inert atmosphere. The resulting anion-radicals (probably because of complexation with zinc ions) become stable enough in air. This is in contrast to the high sensitivity of the same anion-radicals to oxygen in air when they are obtained with the help of alkali metals in ether solvents. Hence, the method based on reduction by Zn/OH system in DMSO gives a tempting alternative to common methods of anion-radical preparation. Furthermore, this method allows one to perform the transfer of only one electron and, in a sense, has advantages over preparative electrolysis at controlled potentials. At the same time, the method remains a purely chemical one, which requires no complicated and expensive instrumentation.

Samarium diiodide (SmI_2, the Kagan reagent) represents another principal example of concerted reduction and complexation. This salt is very easily prepared in THF from samarium finely grounded as a powder, and diiodomethane, diiodoethane, or iodine (Krief and Laval 1999). Samarium iodide can be stored in 10^{-1} M THF solution under an atmosphere of nitrogen or, better, argon (Kagan et al. 1981). It is well known to have exceptional qualities as a single-electron transfer reductant. For species soluble in organic medium, it submits a reduction potential that is negative



SCHEME 1.46

enough ($E_{1/2}$ = −1.62 V in AN versus the saturated calomel electrode; Kolthoff and Coetzee 1957). Like other lanthanide derivatives, SmI_2 presents a high coordination number (usually 7). Therefore, it provides a unique opportunity to include molecules of reactants, solvents, and electron-transfer products in the framework of one subunit (Kagan et al. 1981, Yacovan et al. 1996). This facilitates electron transfer and changes some of the usual reactions of an intermediate radical $R^•$: No coupling product R–R is obtained as a result of the reaction between alkyl halide RX and SmI_2 in THF. The intermediate radical $R^•$ abstracts hydrogen from THF as the only proceeding reaction (Kagan et al. 1981). As a reductant, SmI_2 strictly acts in a one-electron manner. Being reduced by SmI_2, the triselenol cation-radical keeps the integrity of its molecular carcass (Ogawa et al. 1994). Scheme 1.46 illustrates the reaction. (Reduction of selenoorganic compounds is frequently accompanied with partial loss of this heteroatom.)

One-electron reduction by SmI_2 of ortho and para derivatives of acetophenone was studied by Prasad and Flowers (2002). Reactions were performed in dry THF using stopped-flow optical technique. The results show that during one-electron reduction of the substrates, coordination of the carbonyl group to samarium takes place in the cases of para-substituted acetophenones. In the cases of the ortho derivatives, chelation of SmI_2–THF solvate proceeds with participation not only of the carbonyl group but of *o*-substituents as well. Substituents such as fluoro, amino, and methoxy groups participate in the chelation and this is unusual. This chelation enhances the rate of reduction compared to the para-analogues. In particular, the ortho-fluoro substituent on acetophenone enhances the rate of reduction to the highest degree. A review by Dahlen and Hilmersson (2004) describes additives that increase one-electron reductive ability of SmI_2. In particular, the powerful reagent mixture SmI_2/H_2O/amine is presented. Corey and Zheng (1997) used SmI_2 with Zn/Hg to reduce the consumed samarium reagent within the catalytic ternary system.

It would be interesting to examine thulium diiodide in one-electron reduction reactions. On the basis of the work by Evans and Allen (2000), TmI_2 has the potential to be an effective replacement for SmI_2, when the latter is too weak as a reductant, when subambient reaction temperatures are desirable, etc. Perhaps, TmI_2 activity in THF can be controlled by the addition of hexamethylphosphotriamide in the same manner as it regulates power and reactivity of $SmBr_2$ (Knettle and Flowers 2001).

1.8 CONCLUSION

The material discussed in this chapter shows that the organic chemistry of ion-radicals has specific features. The transformation of organic compounds into ion-radicals changes orbital interactions. This causes changes in electron effects of substituents and enhances the ability of a bridge group to participate in electron delocalization. Acid–base properties of organic compounds are also changed fundamentally. This opens new ways to widen the modern methodology of organic synthesis. Based on numerous examples, the chapter proposes ways to enrich the reactivity of metallocomplexes. Comprising an extensive body of work studying organic poly(ion-radical)s of the monomeric

nature, the chapter examines cases of the separate existences of several unpaired electrons and their ferromagnetic coupling. The absence of spin leaking from one ion-radical site to another in the framework of the same molecular skeleton is a very important feature to design organic materials with magnetic properties. In contrast, the section devoted to polymeric ion-radicals describes the approaches to the design conductors that the electronic industry relies on.

Every organic reaction proceeds with the participation of inorganic reagents. Ion-radical organic reactions also have inorganic participants. The chapter discusses inorganic ion-radicals in their reactions with organic substrates. The main aim of this chapter is to lay the basis for all the subsequent chapters.

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2 Formation of Organic Ion-Radicals

2.1 INTRODUCTION

This chapter describes the preparation of organic ion-radicals in relation to its properties, that is, electronic structure, reactivity, and interaction with counterions. In synthetic chemistry of organic compounds, liquid-phase reactions are most typical. Under these reaction conditions, ion-radical salts appear to be surrounded with solvate shells. Solvents can either solvate the individual ions (having cation and anion individually surrounded by solvent molecules) or an ion pair may be solvated as a whole, without solvent molecules between the ions. Further transformations of ion-radicals (their disintegration, interaction with reagents directly or after the disintegration) and formation of transient states and stabilization of final products also take place in solvents. Medium effects on the generation and structure of ion-radicals are of significant interest for experimental and theoretical levels of studies (see, e.g., Orlov et al. 2001). The nature of the solvent defines the efficiency of the chosen method for ion-radical generation. This chapter examines the peculiarities of organic compounds as ion-radical precursors under the conditions of the liquid-phase electron transfer.

Ion-radicals are widely discussed as intermediate products of electrode reactions. Regularities of the electrode reactions are, undoubtedly, important for organic synthesis. At the same time, there are features that are distinctive of the liquid-phase reactions only. The electrode reactions are heterogeneous. There is a strong electric field (10^6–10^7 $V \cdot cm^{-1}$) in the preelectrode (double layer) region. Obviously, this may sometimes affect the reactivity of a depolarizer or an ion-radical originating from it. The solution in the electrode/solution interface region has special (double layer) properties that are significantly different from the bulk. The electrode practically does not change its own properties during reaction with a depolarizer. At a given potential, the influence on species adsorbed on the electrode surface or located in the framework of the double electric layer remains constant. In liquid-phase (homogeneous) reactions, ion-radicals are formed and they react without any influence of either of the electrodes.

Some discrepancy exists between reactions of a donor and an acceptor in their ground states, on one hand, and reactions stimulated by photoirradiation or pulse radiolysis, on the other. The energy of the incoming electron is much higher in photochemistry or pulse radiolysis than in homogeneous electron transfer or processes with participation of an electrode. Of course, the problem of organic ion-radical formation includes both chemical and physical aspects. This book concentrates on chemistry, but includes some physical aspects where necessary for better understanding. Nevertheless, organic photochemistry and radiolysis of organic compounds are very specific branches with their own book repertoire.

Therefore, this chapter provides a summarized data on the preparation of organic ion-radicals as independent particles that can be free or bound with counterions in ion pairs. The chapter considers liquid-phase equilibria in electron transfer reactions and compares electrode and liquid-phase processes for the same organic compounds. Isotope-containing molecules have specific features as ion-radical precursors, therefore, the generation of the corresponding ion-radicals is considered in Section 2.6 of this chapter. This chapter also pays some attention to the peculiarities of ion-radical formation in living organisms.

2.2 CHEMICAL METHODS OF ORGANIC ION-RADICAL PREPARATION

2.2.1 Anion-Radicals

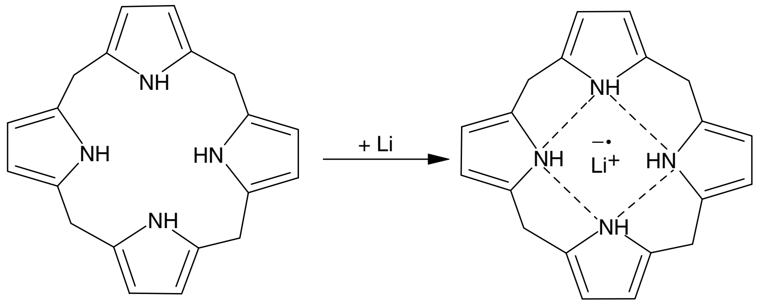
Electrochemical methods for the generation of anion-radicals consist of potential-controlled electrolysis. The control of a potential allows one to detain reduction just after a one-electron transfer to a depolarizer. The one-electron nature of the electron transfer is coincidentally inspected by means of coulombometry. One molecule must consume one electron. If less than one electron is consumed in the framework of the one-electron reduction, it means that the yield of an anion-radical is not quantitative. The electrolysis in a special ampoule placed into a resonator of the electron spin resonance (ESR) spectrometer permits one to identify many unstable anion-radicals. The electrochemical methods of anion-radical generation employ an electrode as an electron donor.

When an alkali metal (M) serves as an electron donor, an acceptor (e.g., ArH) transforms into an ion-radical salt: $M + ArH \rightarrow ArH^{-\bullet}, M^{+}$. Solvation of a resulting M^{+} takes place in a liquid phase. The solvation may play a crucial role in the generation of anion-radicals. For example, benzene, which is a poor electron acceptor, forms its anion-radical by reacting with a potassium mirror in dimethoxyethane (DME). DME solvates potassium cation; the potassium–chelate complex is formed with the participation of two oxygen atoms of the two methoxy groups in each solvent molecule. Solvation of the lithium cation proceeds even more effectively because of the smaller ion radius of lithium than that of potassium. With lithium in DME, the equilibrium concentration of the benzene anion-radical turns out to be two orders higher than that with potassium or sodium (Yakovleva et al. 1960). In brief, the following regularity can be stated: The greater the solvating ability of a medium, the easier is the electron transfer from the same metal to the same organic acceptor.

Diethoxymethane (DEM, $CH_3CH_2OCH_2OCH_2CH_3$) has recently become available in commercial quantities. Although DEM contains a reactive methylene group, namely, $-OCH_2O-$, it is stable to organolithium reagents and, supposedly, can be used for the preparation of anion-radicals. Two important characteristics of DEM that differentiate it from many other ethers are its immiscibility with water and nonhygroscopic nature. For example, DEM from a container that had been open for over a year performed superbly as a solvent for several water-sensitive reactions. With no special drying, it is competitive with "anhydrous grade" tetrahydrofurane (THF), which is usually stored in argon (Boaz and Venepalli 2001).

Another common solvent that contains the oxygen atom easily available for coordination with metal cations is THF. The ability of anion-radicals to remove a proton from the position 2 of THF is sometimes a problem. Dimethyl ether is more stable as a solvent; its oxygen atom is also exposed and can coordinate with a metal cation with no steric hindrance from the framing alkyl groups. An added advantage of dimethyl ether is that, because of its low boiling point (−22°C), it can be readily removed after reductive metallation and replaced by the desired solvent. The use of aromatic anion-radicals in dimethyl ether (instead of THF) is well documented (Cohen et al. 2001, references therein).

The alkali metal reactions with crown ethers and cryptands lead to the formation of salts in which anionic sites are occupied solely by electrons. The salts are called electrides, $Cs^{+}(15\text{-crown-}5)_2 \cdot e$ is a typical example (Dye 2003). However, these conventional organic electrides are thermally unstable at room temperature. The instability is due to reductive cleavage of the C—O bonds of the crown ether in the species formed. Aza[222]cryptand forms stable (at room temperature) electrides with alkali metals, but their energy parameters need to be improved (Kim et al. 1999). Calix[4]pyrrole and lithium can, according to B3LYP calculations by Chen et al. (2005), form an electride of very high energy reserves and stability at room temperature. In this electride, the lithium cation is located in the plane of four nitrogen atoms and the unpaired electron is highly delocalized (see Scheme 2.1). As a consequence, transition energy of the species should be small. It is the lower transition energy that can ensure large first hyperpolarizability. This grounded the expectation of a new type of nonlinear optical material to appear in reality. Such materials have already started to appear (Redko et al. 2005). Because the electrons are weakly bound, electrides exhibit low-energy electron



SCHEME 2.1

emission (Phillips and Dye 2000), which could be useful in devices such as infrared (IR)-sensitive photomultipliers and thermoelectric power or refrigeration sources.

Commonly used alkali metals have lower ionization potentials than reduction potentials, which are needed for the transformation of an organic molecule into its anion-radical. Once a molecule starts getting reduced, it will take up as many electrons as the metal potential allows. For alkali metals, the scope of application is limited to substances for which the first-electron transfer corresponds to enough negative values of cathodic potentials. These first potentials must be highly separated from potentials of the second or, generally, the next electron-transfer steps; if not, metal reduction proceeds deeper. There is no delay in the anion-radical formation. There are reductive reactions that show clear dependence of the homogeneity of a metal reducer. For example, during the alkali metal reduction of bis(*gem*-dihalocyclopropyl)ethane in a mixture of liquid ammonia with THF, the route of any further transformation of primary ion-radicals depends on being an alkali metal in the homogeneous versus heterogeneous phases (Oku et al. 1983). Lithium is dissolved in this mixture, and sodium forms a liquid suspension in it. This determines the general result of the reduction. The presence of sodium metal in the heterogeneous phase leads to adsorption of the substrate on the metal surface. The adsorption creates a high concentration of the reducing metal in the reaction zone. This assists in the deeper reduction resulting in full loss of a halogen. In a homogeneous medium (lithium as a reducer), the rate of primary electron transfer is comparable with the rate of posterior protonation at carbon atoms, and the reaction stops at the stage of elimination of two of the four halogen atoms that are present.

Colloidal potassium has recently been proved as a more active reducer than the metal that has been conventionally powdered by shaking it in hot octane (Luche et al. 1984, Chou and You 1987, Wang et al. 1994). To prepare colloidal potassium, a piece of this metal in dry toluene or xylene under an argon atmosphere is submitted to ultrasonic irradiation at ca. 10°C. A silvery blue color rapidly develops, and in a few minutes the metal disappears. A common cleaning bath (e.g., Sonoclean, 35 kHz) filled with water and crushed ice can be used. A very fine suspension of potassium is thus obtained, which settles very slowly on standing. The same method did not work in THF (Luche et al. 1984). Ultrasonic waves interact with the metal by their cavitational effects. These effects are closely related to the physical constants of the medium, such as vapor pressure, viscosity, and surface tension (Sehgal et al. 1982). All of these factors have to be taken into account when one chooses a metal to be ultrasonically dispersed in a given solvent.

Several methods have been reported for the preparation of highly reactive metal powders by reduction of metal salts in ethereal or hydrocarbon solvents. These methods used powdered alkali metals as reducing agents in conjunction with or without an electron carrier of the naphthalene type (e.g., Yang et al. 2006). The reduction of metal salts in this manner produces finely divided metal slurries. The slurries are highly reactive, air sensitive, and usually pyrophoric in the absence of a solvent. Active magnesium, zinc, indium, copper, and other metals were prepared in this way (Yus 1996, Rieke and Hanson 1997). The metals were used for the hydrogenation of alkynes to alkanes (Alonso and Yus 1997) or for the addition of highly reactive zinc to organic bromides

(Guijarro et al. 1999). These active metallic forms can, obviously, be utilized in special cases of anion-radical preparation, although there is no mention of this in cited works.

By and large, a finely divided precipitate of a metal is a very effective one-electron reducer. For example, a finely divided precipitate of Zr(0) was obtained on mixing naphthalene sodium derivative in THF with $ZrCl_4$. The Zr(0) precipitate dissolved on addition of anthracene or benzophenone to form the corresponding zirconium salts of the anion-radicals (Terekhova et al. 1996).

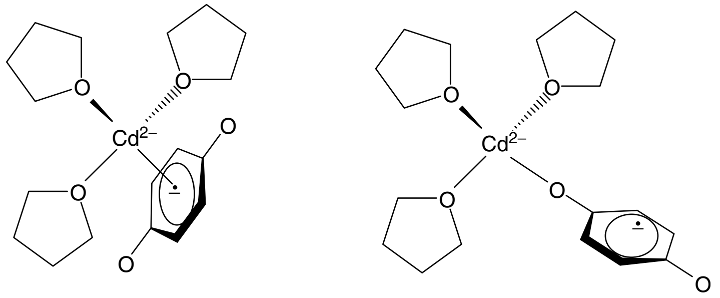
Neutral organic molecules can also be one-electron donors. For example, tetracyanoquinodimethane gives rise to anion-radical on reduction with 10-vinylphenothiazine or *N*,*N*,*N*′,*N*′-tetramethyl-*p*-phenylenediamine. Sometimes, alkoxide or phenoxide anions find their applications as one-electron donors. There is a certain dependence between carbanion basicity and their ability to be one-electron donors (Bordwell and Clemens 1981).

An unusual case of anion-radical preparation consists of reduction of 4- and 3-nitrocatechol or nitrohydroquinone with sodium borohydride in air and in aqueous solutions. The resulting anion-radicals are stable at pH 9–12 despite the presence of water (Grenier et al. 1995).

As already stated, the interaction between the metal cation and anion-radical formed is usually a simple ion association moderated by the Coulombic attraction between the two species and competitive ion-solvating nature of the given solvent. However, interaction between organic one-electron acceptors and some metals results in the formation of a special class of organometallic complexes. The metals reduce the acceptor molecules. The anion-radical and cation forms a coordination anion-radical complex. In the case of one-electron reduction by cesium metal in the presence of 18-crown-6-ether, 9-fluorenyl-4-toluyl methane forms an anion-radical salt. In this salt, the anion-radical expresses large affinity for the cesium cation. The anion-radical affinity for the cesium cation exceeds the crown affinity, and Cs^{1+} is placed between the fluorenyl and toluyl π systems. Having the exocyclic methylene group as a stopper, the fluorenyl and toluyl fragments come closer together and make a cleft, which is appropriate, in terms of dimensions, for cesium cation. The potassium and sodium cations do not get such a preference. ESR experiments and B3LYP calculation testify for π−*s*−π delocalization of an unpaired electron in the anion-radical salt as discussed. In other words, the delocalization proceeds with the participation of the two π contours of the aromatic parts and the *s* orbital of the cesium cation (Stevenson et al. 2006).

When Cd ($d^{10}s^2$) metal reduces benzoquinone in THF, a solvated organometallic compound is formed (Stevenson et al. 1995). According to ESR studies, the benzosemiquinone anion-radical is associated with Cd^{2+} ion or coordinated to it (see Scheme 2.2).

Exposure of naphthalene dissolved in liquid ammonia to europium metal immediately results in the characteristic green color of naphthalene anion-radical. ESR analysis reveals a signal that comes from an unpaired electron interacting with ^{151}Eu and ^{153}Eu nuclei. No hyperfine coupling with naphthalene protons is observed, although treatment with water leads to 1,4-dihydronaphthalene (Stevenson et al. 1999). This means that naphthalene has indeed been reduced to its anion-radical and undergone a normal Birch reaction. These results are consistent with the initial donation of two



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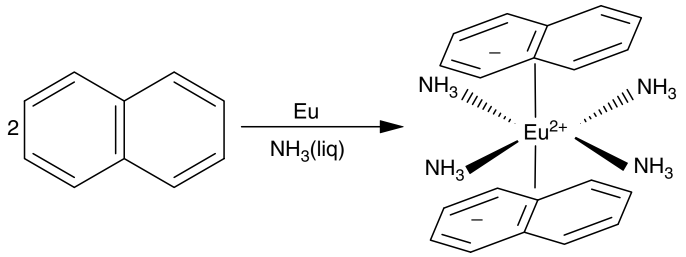


SCHEME 2.3

s electrons to two acceptor molecules. Tight coordination then takes place between the two naphthalene anion-radicals and the central atom of Eu^{2+}, presumably through the europium *s* orbital. Since the two electrons, donated by Eu, are in the same molecular orbital, they are spin paired. Hence, only the remaining seven unpaired *f* electrons can contribute to the ESR signal. Therefore, the resulting ESR spectrum reflects the interaction of europium nucleus with a single electron spin. The structure of the complex is depicted in Scheme 2.3.

The structure "is tentative, but it is known that (1) europium ions prefer an octahedral geometry, (2) they complex well with ammonia, and (3) (in this case) two naphthalene units are involved" (Stevenson et al. 1999).

Sanyal et al. (2004) reported another unusual example of anion-radical generation during coordination to a metal in the presence of a reductant. In their reaction, ammonium heptamolybdate, $(NH_4)_6[Mo_7O_{24}]$, and 2-[(aryamino)phenylazo]pyridine (the ligand L) on reductive action of triphenylphosphine was converted into the oxo-free $(L^{-\bullet})Mo^{IV}(L^{\bullet})$ complex. The complex was diamagnetic at ambient temperature. Obviously, antiferromagnetic coupling takes place in the $(L^{-\bullet})Mo^{IV}(L^{\bullet})$ complex with participation spins of the anion-radical ligands and one vacant orbital of the central metal atom.

Reactions of cobalt porphyrin with *p*-fluoranyl or phenyl-*N*-butylimidazole proceeds analogously—both fluoranyl and imidazole coordinate with the cobalt contained in the porphyrin complex, but fluoranyl was fixed in its semiquinone, anion-radical form (Okamoto and Fukuzumi 2003).

Sometimes, the anion-radical salts formed in a solution crystallize as aggregates (Bock et al. 2000a). Thus, anthracene was reduced by sodium in triglyme or by potassium in THF. Structures of the corresponding crystalline anion-radical salts were established by x-ray analysis. As it turned out, the anthracene reaction with sodium in triglyme led to the formation of anion-radical salt with the sodium cation surrounded by two triglyme molecules. In the K + THF system, the ionic quadruple of two anthracene anion-radicals connected by a $[(K^+)_2(THF)_3]$ bridge crystallizes (Bock et al. 2000b). As seen, the nature of cation and solvent effects define the type of stabilization for the same anion-radical.

Many dihydroxyquinones can bind to a metal cation in the well-known chelation fashion. Magnesium (2+) forms chelates with 5,8-dihydroxynaphtho-1,4-quinone and 1,4-dihydroxyanthra-9,10-quinone. These chelates are stable and characterized by large formation constants. When the corresponding semiquinones (anion-radicals) form complexes with magnesium (2+), the stability constants become too small. This apparent paradox is explained by the much stronger intramolecular hydrogen bonding existing in hydroxysemiquinones when compared to neutral quinones (Alegria et al. 2000).

2.2.2 Cation-Radicals

To understand features of oxidative one-electron transfer, it is reasonable to compare average energies of formation between cation- and anion-radicals. One-electron addition to an organic molecule is usually accompanied by energy decrease. The amount of energy reduced corresponds to

the molecule's electron affinity. For instance, one-electron reduction of aromatic hydrocarbons can result in energy revenue of 10–100 kJ mol^{-1} (Baizer and Lund 1983). If a molecule detaches one electron, mostly energy absorption takes place. The needed amount of energy consumed is determined by the molecule's ionization potential. Particularly, ionization potentials of aromatic hydrocarbons vary from 700 to 1000 kJ mol^{-1} (Baizer and Lund 1983).

Studies in cation-radical chemistry began with works by Weiss (1941) and Michaelis et al. (1941). However, intense investigations in this field started after instrumental methods emerged (ESR and optical spectroscopy in particular). Optical spectroscopy revealed a very intriguing case where direct sublimation of methylviologen (1,1′-dimethyl-4,4′-dipyridinium) dichloride provokes the formation of methylviologen cation-radical monochloride. This phenomenon was established by Poizat et al. (1984), but remains unexplained.

As observed, aromatic hydrocarbons gave products of protonation on dissolution in hydrofluoric acid. Oxidation into aromatic cation-radicals did not take place (Kon and Blois 1958). Trifluoroacetic acid is able to transform aromatics into cation-radicals. This acid is considered a middle-powered one-electron oxidant (Eberson and Radner 1991). Its oxidative ability can be enhanced in the presence of lead tetraacetate. This mixture, however, should be used carefully to avoid oxidation deeper than the one-electron removal. Thus, oxidation of 1,2-phenylenediamine by the system $Pb(OCOCH_3)_4 + CF_3COOH + CH_2Cl_2$ leads to the formation of either primary or secondary cation-radicals. The primary product is the cation radical of initial phenylenediamine, whereas the secondary product is the cation radical of dihydrophenazine (Omelka et al. 2001). Sulfuric acid is also used as an one-electron oxidant, especially for aromatic hydrocarbons. In this case, generation of cation radicals proceeds simultaneously with the hydrocarbon protonation and sulfonation (Weissmann et al. 1957).

Anodic oxidation in inert solvents is the most widespread method of cation-radical preparation, with the aim of investigating their stability and electron structure. However, saturated hydrocarbons cannot be oxidized in an accessible potential region. There is one exception for molecules with the weakened C—H bond, but this does not pertain to the cation-radical problem. Anodic oxidation of unsaturated hydrocarbons proceeds more easily. As usual, this oxidation is assumed to be a process including one-electron detachment from the π system with the cation-radical formation. This is the very first step of this oxidation. Certainly, the cation-radical formed is not inevitably stable. Under anodic reaction conditions, it can expel the second electron and give rise to a dication or lose a proton and form a neutral (free) radical. The latter can be either stable or complete its life at the expense of dimerization, fragmentation, etc. Nevertheless, electrochemical oxidation of aromatic hydrocarbons leads to cation-radicals, the nature of which is reliably established (Mann and Barnes 1970; Chapter 3).

In majority of cases, the electrochemical generation of organic cation-radical takes place in an ampoule lowered into an ESR cavity. Sometimes, however, exhaustive external generation and the use of a flow system allows one to obtain an ESR spectrum that is far better resolved (see, e.g., Seo et al. 1966). Electrochemical methods are very useful in structural studies but are barely applicable in preparative aims. This is due to the limited stability of cation-radicals. It is difficult to carry out low-temperature preparative electrolysis, and the main problem is the disposal of the large amount of heat generated during the electrode work. That is, not much current can be passed through an ordinary-sized electrode without generating too much heat. When the potential and temperature control are necessary, only small quantities of material can be obtained within a reasonable period of time. When potential and temperature control is not necessary, as in Kolbe electrolysis, anodic oxidation is indeed useful as a preparative method.

As for chemical paths to cation-radical generation, the following oxidants deserve to be mentioned: concentrated (98%) sulfuric acid (Carrington et al. 1959, Hyde and Brown 1962, Carter 1971), persufate (Minisci et al. 1983), iodosobenzene bis(trifluoroacetate) (Alberti et al. 1999), and chlorine dioxide (Handoo et al. 1985, Sokolov et al. 1999). The following metal ions were used in many applications: Tl(III) (Elson and Kochi 1973, McKillop and Taylor 1973), Mn(III) (Andrulis

et al. 1966), Co(III) (Kochi et al. 1973), Ce(IV) (Norman et al. 1973), Ag(I) and Ag(II) (Nyberg and Wistrand 1978), and Pd(II) (Eberson and Wistrand 1980). Methods of cation-radical generation have also been developed in which oxidants are $SbCl_5$ (Ishizu et al. 1973), $AlCl_3$ (Forbes and Sullivan 1966), I_2 (Stamirez and Turkevich 1963), $Pb(OAc)_4$ (Elbl-Weiser et al. 1989), and XeF_2 (Shaw et al. 1970). Potassium 12-tungstocobaltate was also described as a strictly one-electron oxidant for organic substances (Eberson 1983, Baciocchi et al. 1993).

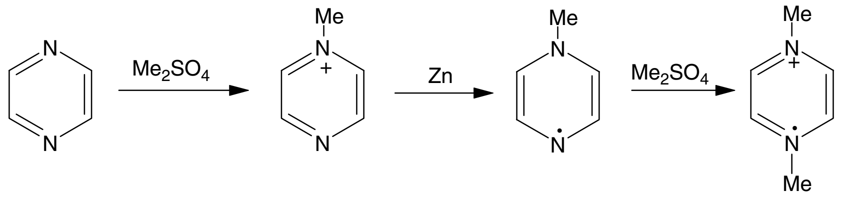
This list of oxidants should be complemented by considering the regularities of their actions (see Chapters 1, 4, and 7). Here, the following three oxidants ought to be emphasized: $Ar_3N^{+\bullet}SbCl_6^-$, NO^+, and Ag^+. Tris(bromophenyl)amine is now available commercially; when oxidized with $SbCl_5$, it forms tris(bromophenyl)ammoniumyl hexachloroantimonate. The $NO^+PF_6^-$ and $NO^+BF_4^-$ salts are also available; they are especially convenient for the isolation of oxidized products. This is because the reduction product evolved, $NO^\bullet$, is a gas. The Ag^+ is used whenever the compounds are easy enough to oxidize—the reduced form is separable solid silver (often as a mirror on the reaction vessel walls). Like NO^+, Ag^+ is characterized by a high sensitivity of its standard redox potential to the nature of the solvent. (For selecting chemical oxidants and reductants, see review by Connelly and Geiger (1996).)

In some cases, cation-radicals are formed from neutral organic molecules by the action of neutral organic acceptors such as tetracyanoethylene, tetranitrofluorenone, quinones, and free radicals—aroxyls, nitroxyls, and hydrazyls.

As discussed, there are various methods of cation-radical generation. Every individual case needs its own appropriate method. A set of these methods is continuously being supplemented. For example, it was very difficult to prepare the cation-radicals of benzene derivatives with strong acceptor groups. However, some progress has been achieved, thanks to the use of fluorosulfonic acid, sometimes with addition of antimony pentafluoride, and lead dioxide (Rudenko 1994). As known, superacids stabilize cationic intermediates (including cation-radicals) and activate inorganic oxidants. The method mentioned is effective at $-78°C$. Meanwhile, $-78°C$ is the boundary low temperature because the solution viscosity increases abruptly. This leads to the anisotropy of a sample and a sharp deterioration in the ESR spectrum quality.

Another example involves the preparation of cation-radicals from aromatic hydrocarbons. In concentrated sulfuric acid or in a mixture of antimony pentachloride with methylene chloride, polyacenes give cation-radicals with ill-resolved ESR spectra (Lewis and Singer 1965). The employment of molten antimony trichloride at $+80°C$ results in an improved resolution and diminution of line widths up to the ideal value of 0.005–0.008 mT (Buchanan et al. 1980). Under these conditions, even naphthalene gives cation-radical, with an ESR spectrum of very good quality. The mentioned spectrum surprisingly describes the naphthalene cation-radical in its monomeric (not dimeric) form. An essential peculiarity of the method is its special opportunity to regulate the oxidation capacity of $SbCl_3$. It is sufficient to add several mole percent of a chloride acceptor (e.g., $AlCl_3$) or a chloride donor (e.g., Me_4NCl). Because the oxidation process is reversible, a measure of its reversibility is the yield of antimony in the zerovalent state: $SbCl_3 + 3ArH = 3(ArH)^{+\bullet} + 3Cl^- + Sb^0$. Bringing Cl^- out of the reaction sphere (by the addition of $AlCl_3$) leads to an increase in $(ArH)^{+\bullet}$ concentration. Getting Cl^- into the reaction sphere (by the addition of Me_4NCl) leads to a decrease in $(ArH)^{+\bullet}$ concentration. As seen, the equilibrium between starting substances and electron-transfer products can be very important, especially for homogeneous reactions. The depicted equilibrium may be more complex in reality and include polyantimonium polyhalides, but the most important peculiarity is the possibility of regulating the oxidative capacity as shown here.

Other methods for the generation of cation-radicals should also be mentioned. Mesoionic 5,5'-azinobis(1,3-diphenyltetrazole) and related mesoionic compounds give cation-radicals on oxidation by lead tetraacetate. The reaction proceeds in the presence of sodium tetrafluoroborate. The tetrafluoroborate cation-radical salt is stable and can be purified by column chromatography on silica gel and stored in air for several months without appreciable decomposition (Araki et al. 1999). The cation-radicals of *N*,*N'*-dimethyldiazines are produced by usual oxidation of the parent diazine



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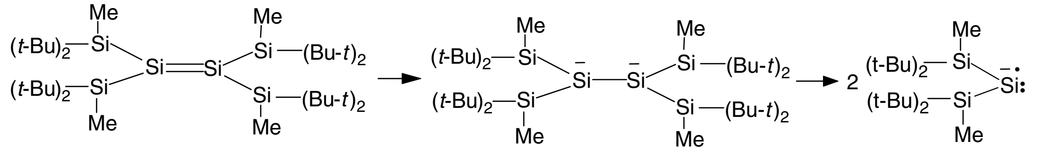


SCHEME 2.5

(Soos et al. 1977) as well as by reduction of the corresponding diquarternary salts (Schulz et al. 1988). The viologen cation-radicals are also obtained by one-electron reduction of viologens, which are the dications. Lucarini et al. (1994) elaborated a one-pot method for generating cation-radicals from corresponding aromatic bases by the action of dimethyl sulfate, Me_2SO_4, as a methylating agent and zinc powder as a reductant. The reaction proceeds in benzene as shown in Scheme 2.4.

Another variant of the reductive method to produce cation-radicals consists of the initial removal of a function of good fugacity present in α,β-functionalized alkanes. This generates a radical center at the α position, which assists in the elimination of another function from the β position. The remaining function departs as an anion, leaving the organic framework in the form of a cation-radical. A detailed review of this method is presented by Crich et al. (2006). This method is represented by a generic equation:

$$>C(NO_2)\text{–}C(OMes)< \rightarrow NO_2^- + >{}^{\bullet}C\text{–}C(OMes)< \rightarrow MesO^- + >{}^{\bullet}C\text{–}C^+<$$

2.2.3 Carbenoid Ion-Radicals

This class of ion-radicals is characterized by the localization of an unpaired electron at the atom bearing a free (valence) electron pair. Although their applicability in organic synthesis remains an open question, the preparative methods and electron structure of carbene ion-radicals attract some attention of the researchers. Probably, it is an initial step to a new chapter in organic ion-radical chemistry.

Several examples of carbenoid ion-radicals are discussed within this book. A silylene anion-radical preparation and properties is exemplified here. Scheme 2.5 shows the path to this species. Tetrakis(di-*tert*-butylmethylsilyl)disilylene was reduced by lithium or sodium salt of naphthalene anion-radical in THF at −78°C and then 12-crown-4 was added to the resulting reaction mixture. The silylene anion-radical was obtained as the corresponding alkali salt. Red crystals of the salt were isolated and characterized by ESR spectroscopy and x-ray crystallography (Inoue et al. 2007).

The authors proposed the following picture of the silylene anion-radical formation. Treatment of the starting material by the naphthalene anion-radical salt with lithium or sodium (the metals are denoted here as M) results in two-electron reduction of >Si=Si< bond with the formation of >SiM–MSi< intermediate. The existence of this intermediate was experimentally proven. The crown ether removes the alkali cation, leaving behind the $>Si^-\text{—}^-Si<$ counterpart. This sharply increases electrostatic repulsion within the silicon–silicon bond and generates the driving force for its dissociation. In a control experiment, with the alkali cation inserted into the crown ether, $>Si^-\text{—}^-Si<$ species does dissociate into two $[>Si:]^{-\bullet}$ particles.

2.3 EQUILIBRIA IN LIQUID-PHASE ELECTRON-TRANSFER REACTIONS

Let us consider a redox reaction of the following type: $A^{-\bullet} + B = A + B^{-\bullet}$. In this reaction, $A^{-\bullet}$ acts as a one-electron donor and transforms into A. At the same moment, B gives rise to $B^{-\bullet}$. If the reaction is reversible, the equilibrium is the sum of the following two processes: $A^{-\bullet} = A + e$ and $B + e = B^{-\bullet}$. Electrochemically, both processes are expressed by their standard potentials E^0(A) and E^0(B). To consider some polarographic studies, let us note that polarographic half-wave potentials $E_{1/2}$(A) and $E_{1/2}$(B) can, under certain conditions, be used instead of E^0(A) and E^0(B). Namely, if both processes are one-electron in nature and they are fast and reversible, their $E_{1/2}$ values are equal to those of standard redox potentials (referring to the conditions used in a given electrochemical experiment). Values of $E_{1/2}$ show how easily A or B accepts an electron, that is, these values describe the acceptor/donor ability of A or B. The equation $\log K = F[E_{1/2}(A) - E_{1/2}(B)]/RT$ counts equilibrium constants (K) using Faraday's constant (F) and $E_{1/2}$ values of one-electron reversible polarographic waves for A and B (Gennaro et al. 1988). From the equation $E_{1/2}$(A) value can be calculated if $E_{1/2}$(B) and K are known.

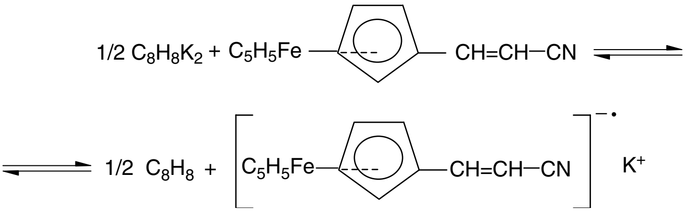
This estimation has been made for a reaction between the anion-radical of tetracyanoquinodimethide (TCNQ) and 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ; Iida and Akamatu 1967): $(TCNQ)^{-\bullet} + DDQ = TCNQ + (DDQ)^{-\bullet}$. The equilibrium constant of the reaction was determined spectrometrically in AN. Having K and $E_{1/2}$(DCNQ) as the known values, $E_{1/2}$(TCNQ) was determined to be 38 mV. The experimental (polarographic) value was 40 mV. As seen, the calculated and experimental values turned out to be close.

Hence, equilibrium constants of homogeneous electron-transfer reactions between $(A)^{-\bullet}$ and B are evidently connected with a difference in reduction potentials of A and B. This connection reflects a definite physical phenomenon. Namely, if two redox systems are in the same solution, they react with each other until a unitary electric potential is reached. For the transfer of only one electron at room temperature, the equation $\log K = 2.3\ [E_{1/2}(A) - E_{1/2}(B)] \cdot 0.059$ can be employed.

The applicability of this simple equation has been checked for one principally important case concerning the electron exchange between species belonging to quite different classes of chemical compounds. Cyclooctatetraene dipotassium and β-ferrocenylacrylonitrile as donor and acceptor, respectively, react in THF. The reaction is reversible, and the presence of all the four components has been proved (Todres 1987). Scheme 2.6 illustrates the equilibrium.

According to C_8H_8 yield and concentrations of the four components, the equilibrium constant of the reaction in Scheme 2.6 was determined as 4×10^{-2}. The value calculated from the potential difference was 4.4×10^{-2}. Consequently, there is a coincidence between the calculated equilibrium constant based on the electrode potentials and the equilibrium constant determined from the liquid-phase experiment.

In all of the examples considered, $E_{1/2}$ of the acceptor was much more negative than that of a donor. In liquid phase, one-electron transfer from a donor to an acceptor can, however, proceed even with an unfavorable difference between these potentials if the system contains the third component—the so-called mediator. The mediator is a substance capable of accepting an electron from a donor and sending it instantly to an acceptor.



SCHEME 2.6

As an example, the reaction of tetrachloromethane with *N,N,N′,N′*-tetramethyl-1,4-phenylenediamine (TMPDA) can be discussed. The presence of *p*-benzoquinone (Q) in the system provokes electron transfer (Sosonkin et al. 1983). Because benzoquinone itself and tetramethyl-*p*-phenylenediamine interact faintly, the effect is evidently a result of redox catalysis. The following equations reflect such kind of catalysis:

$$CCl_4 + TMPDA \rightarrow (TMPDA)^{+\bullet} + Cl^- + {}^{\bullet}CCl_3$$

$$TMPDA + Q \rightarrow (TMPDA)^{+\bullet} + Q^{-\bullet}$$

$$Q^{-\bullet} + Q^{-\bullet} = Q + Q^{2-}$$

$$Q^{2-} + CCl_4 \rightarrow {}^{\bullet}CCl_3 + Cl^- + Q^{-\bullet}$$

$$Q^{-\bullet} + {}^{\bullet}CCl_3 \rightarrow Q + {}^{-}CCl_3$$

$${}^{-}CCl_3 + H^+ \rightarrow CHCl_3$$

The observed catalytic effect can be explained by comparing the redox potentials of the reacting species. The potentials of the reversible electron transfers from TMPDA to Q and then from $Q^{-\bullet}$ to $Q^{-\bullet}$, too with the formation of Q^{2-} are right in the middle of the gap between the potentials of CCl_4 and TMPDA. This leads to dividing the gap into three components so as each of the divided one occurs to be gotten over readily.

It needs to be noted that $Q^{-\bullet} + Q^{-\bullet} = Q + Q^{2-}$ equilibrium is possible due to the rapid consumption of Q^{2-} reducer. More often, the interaction of two identical ion-radicals can lead to their dimerization, but not disproportionation. For instance, the anion-radicals of tetracyanoethylene undergo dimerization (Lu et al. 2003). According to Miller and Novoa (2007), this dimerization proceeds as four-center carbon–carbon bonding. Rosokha and Kochi (2007) proposed the term "π interaction" for dimerization of the cation-radicals of tetrathiafulvalene. Because the π dimers are double-charged species, solvent polarity is essential for their formation. The π interaction overcomes the electrostatic repulsion, even in moderately polar environments.

A curious case of the effect of light on electron-transfer equilibrium concerns the reduction of α,β-di(*tert*-butyl)stilbene with potassium in DME. The reaction leads directly to a diamagnetic dianion; a solution of this dianion remains ESR-silent unless subjected to ultraviolet irradiation by a Hg/Xe lamp. The anion-radical of α,β-di(*tert*-butyl)stilbene is then formed from the dianion by loss of an electron. The electron reverts within 5–10 min after ultraviolet irradiation is turned off, transforming the anion-radical into the dianion (Gerson et al. 1996). This case needs to be brightened. Maybe, the light effect consists simply of singlet–triplet transformation of the dianion with the formation of a more or less stable biradical state of the dianion, which possesses two unpaired electrons, and can be a paramagnetic one.

Julliard and Chanon (1983), Chanon et al. (1990), and Saveant (1980, 1993) developed redox catalysis largely for use in electrochemistry. Using naphthalene and the naphthalene anion-radical as a mediating system, Matsunaga and Yasuhara (2005) performed the environmentally essential dechlorination of polychlorobiphenyls by electrolysis in dimethylformamide (DMF). Polychlorobiphenyls are transformed into their anion-radicals, which eliminate chlorine completely. It needs to be noted that polychlorobiphenyls were widely used as insulating liquids in electrical equipment. However, they have been linked to increased risk of several types of cancer. Despite their usage being limited now, they remain one of the most important groups of persistent pollutants to which humans are exposed, primarily through dietary intake and water pollution. Because of their oxidative and thermal stability, high energy is required to destroy them by thermolysis. Also, it is necessary to carefully control the thermolysis conditions to avoid the formation of polychlorinated dibenzodioxines and dibenzofurans, which are even more dangerous than the parent polychlorocompounds. In contrast, the anion-radical-mediated reductive method offers relatively mild conditions for selective (and complete) dechlorination.

2.4 ELECTROCHEMICAL METHODS VERSUS CHEMICAL METHODS

To date, the results of chemical and electrochemical studies have generally been considered in isolation. The purpose of this section is to present a digest of data obtained by the two methods in an effort to demonstrate that a great deal may be gained by both chemical and electrochemical means rather than any one of the methods, as is the currently accepted practice.

In the electrochemical technique, the electrode provides the source (reduction) or sink (oxidation) for electrons. Variation in the applied potential provides the driving force, which enables the redox reaction to occur. An organic depolarizer diffuses toward the electrode surface, enters the double layer region, and accepts one electron from the cathode or transfers its own electron to the anode. After this, further electrode processes take place within the double layer or a chemical transformation proceeds far from the electrode surfacef, in the bulk solution.

In homogeneous redox reactions, organic ion-radicals are formed at the final stage of donor–acceptor (D–A) interactions: $D + A = D^{\delta+}, A^{\delta-} = D^{+\bullet}, A^{-\bullet} = D^{+\bullet} + A^{-\bullet}$. All such bimolecular reactions include encounter complexes, involving a transfer of as much electron density as needed to stabilize the system, the amount varying widely depending on what the two molecules are. When there is a lot of density transfer, it is certainly reasonable to call the encounter complex a charge-transfer complex. The equilibrium constants for complex formation are supposed to vary smoothly from small to large, depending on what the reacting molecules are. It is worthwhile to consider the products of donor–acceptor interaction, namely, charge-transfer complexes and ion-radicals.

With regard to electrochemical reactions, ion-radicals are well-known primary products. Charge-transfer complexes are more usual for chemical processes, but they have their own analogy in electrochemistry—the formation of a charge-transfer complex is in a certain sense similar to the formation of an electrode-substrate complex. As an example, aromatic, especially polycyclic, hydrocarbons are adsorbed on platinum and other metal anodes with adsorption enthalpies ranging from -25 to $-42\ \mathrm{kJ \cdot mol^{-1}}$. As calculated, this adsorption must occur with the π-electron contour parallel to the surface. The type of bonding involved would be of the same kind as that in a π complex. The distance between the hydrocarbon molecule and surface would probably be of the same magnitude as that in π-donor–π-acceptor complexes, or approximately 0.35 nm (Baizer and Lund 1983). The adsorption of supporting electrolyte or other additives can create a special microenvironment in the reaction layer near the electrode, which can favor distinct pathways. Thus, the use of tetraalkylammonium ions as supporting electrolyte depletes the electrode surface of a solvent and sometimes encourages the products of electron transfer to react, with no solvent participation.

The intermediates generated at the surface diffuse into the bulk solution. Owing to their high reactivity, the intermediates react in a fairly thin reaction layer that adheres to the electrode, and thus their concentration is higher than in homogeneous reactions where they spread uniformly over the medium. This can influence the nature of the product and its distribution.

The fundamental electrochemical event, that is, electron transfer, occurs at the electrode surface. Peculiarities of electrochemical reactions include an electrical field, which in a special way complicates the phenomena of adsorption and desorption at the surface. The first layer of the solution, which is in contact with the electrode, possesses a specific structure. It is important for charged particles that the orientation of medium molecules in the vicinity of the electrode produces a decrease in dielectric permeability in the compact part of the double layer (Damaskin and Kryshtalik 1984).

Substrate and intermediate species adsorb on an electrode surface and orient themselves so that their least hindered sides face the electrode, unless there is another effect such as a polar one. An electrode interface has a layered structure in which a nonuniform electric field (some slope of potential) is generated by polarization of the electrode. An extremely strong electric field of approximately $10^8\ \mathrm{V\ cm^{-1}}$ in the innermost layer might cause a variety of polar effects. For instance, electrochemical one-electron oxidation of *o*-aminophenol derivatives proceeds adiabatically. On the contrary, the homogeneous reaction is nonadiabatic. This difference in behavior is related to

the fact that electrode reaction takes place in a strong electric field that stabilizes the zwitterionic form of the reactant. In this form, the proton has been transferred from the hydroxy to amino group, before oxidation. In the homogeneous reaction, the two processes—removal of an electron from the NH_2 group and proton transfer from OH to $NH_2^{+\bullet}$—go on concertedly (Costentin et al. 2007). This homogeneous reaction represents proton-coupled electron transfer.

Since not only the electron-transfer step but also adsorption and some of the chemical steps involved in an electrode reaction take place in the layer, the whole process should be strongly influenced by polar factors. The orientation of polar-adsorbed species, such as ion-radicals in particular, is electrostatically influenced, and consequently, the stereochemistry of their reactions is also controlled by such kind of electrostatic factor. All these phenomena have been summarized in several monographs. The collective volume edited by Baizer and Lund (1983) is devoted to organic electrochemistry. This issue is closer to the scope of our consideration than its latest version edited by Lund and Hammerich (2001) (these editors have changed the invited authors and, consequently, the chapters included).

As for chemical reactions, the reduction/oxidation (redox) reactions in an homogeneous medium (i.e., in the bulk of the solution) have been experimentally studied with proper intensity only in the past decades. There has been some development of the bulk reactions. However, as earlier, a comparison of the same compound in chemical and electrochemical electron/charge-transfer reactions is still of current interest. Such a comparison is made in this section. The examples offered are intended to invoke novel interpretations or discover new colors in pictures, which have already been drawn.

2.4.1 Charge-Transfer Phenomena

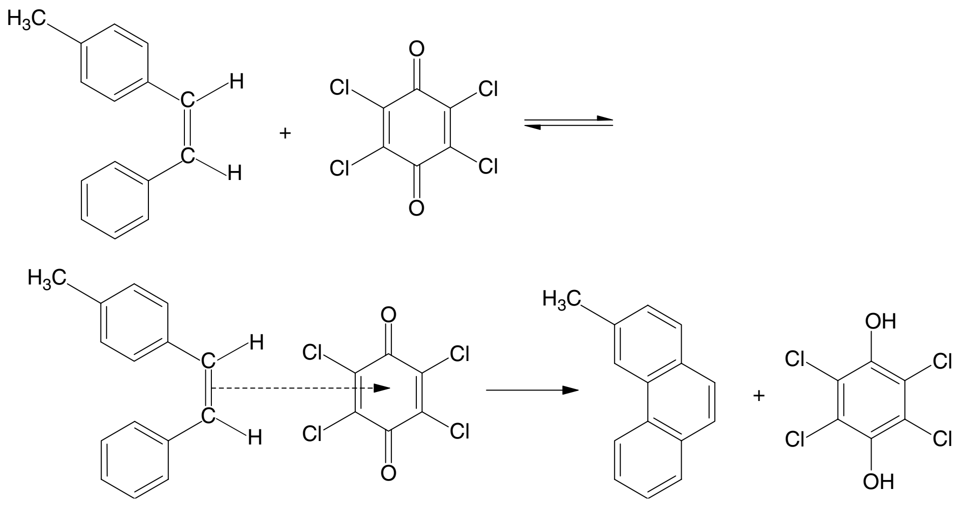
It is worth noting that there is a significant difference between the conversion of the same substrate under one-electron (electrode) transfer and charge-transfer complexes (homogeneous medium).

Anodic oxidation of tetraphenylethylene at a platinum electrode leads to the product of cyclization, namely, 9,10-diphenylphenanthrene (Stuart and Ohnesorge 1971).

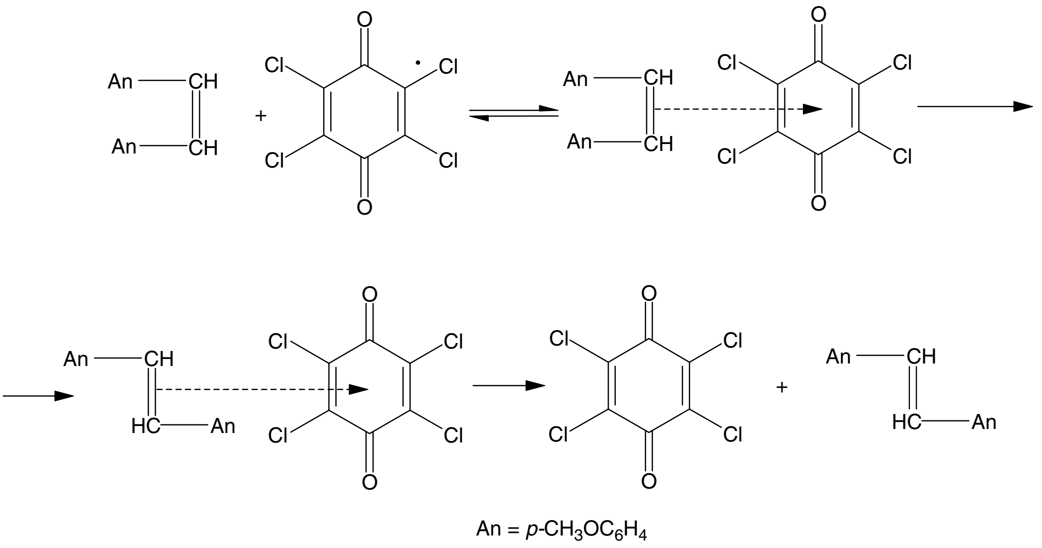
The intramolecular coupling reaction does not occur when diphenylethylenes, that is, stilbene and its methyl derivatives, are electrolyzed under the same conditions (Stuart and Ohnesorge 1971). This difference in the anodic behavior of these substances was attributed to the low stability of the cation-radicals of stilbene and its methyl derivatives in comparison to the cation-radicals of tetraphenylethylene. The participation of the cation-radicals in the cyclization of tetraphenylethylene has been unequivocally proved (Svanholm et al. 1974, Steckhan 1977).

In homogeneous conditions, when *p*-chloranil plays the role of electron acceptor, 4-methylstilbene (α-phenyl-β-tolylethylene) can, however, be cyclized and converted into 3-methylphenanthrene. The reaction takes place by the formation of a charge-transfer complex at a very moderate temperature (36°C) and does not require light radiation (Todres et al. 1990). Scheme 2.7 depicts the transformation in brief.

The behavior of 4,4′-dimethoxystilbene on the electrode and on the action of *p*-chloranil in solutions was compared (Todres and Ionina 1992). It was found that the cis and trans isomers of the compound form different charge-transfer complexes with chloranil, which are unlike in color and can be converted; conversion was found to be in the cis-to-trans direction. Reverse transition was not observed, and cyclization was also not detected (which takes place in case of 4-methylstilbene; Scheme 2.8). Formation of charge-transfer complexes was observed in homogeneous solutions. Because of the limited solubility of chloranil, the reaction was performed in a boiling solvent. In hexane and methylene chloride (boiling points [b.p.] are 69 and 40°C, respectively), the degree of the cis-to-trans conversion was 50 and 30%, respectively. No conversion was observed in the absence of chloranil, when *cis*-dimethoxystilbene was kept in these solvents at the temperatures noted. In case of benzene (b.p. 80°C), no conversion was observed. This is perhaps because benzene competes with dimethoxystilbene in binding with chloranil in a charge-transfer complex much



SCHEME 2.7



SCHEME 2.8

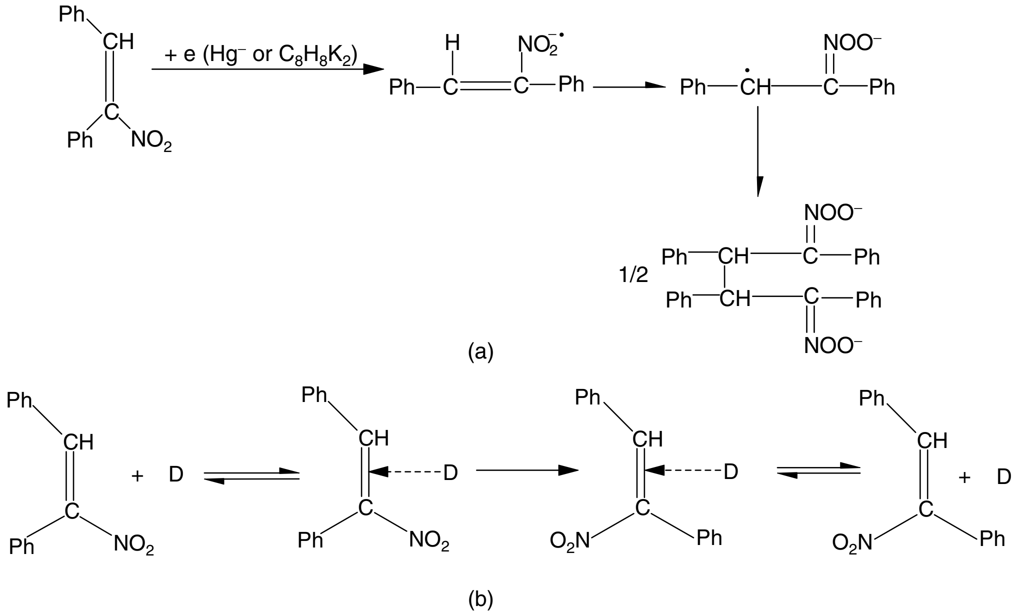
more successfully than the molecules of the other solvents used. This hypothesis is totally logical if we assume that the chloranil acceptor binds in a charge-transfer complex with dimethoxystilbene due to the benzene ring and not because of the ethylene bond (see also Todres et al. 1992a).

During oxidation on a platinum anode, the same 4,4'-dimethoxystilbene yields the cation-radical in the first step. These cation-radicals have a sufficient lifetime and dimerize even in the presence of nucleophiles (Parker and Eberson 1969, Steckhan 1978, Burgbacher and Schaefer 1979) as follows:

$$2\text{AnCH}{=}\text{CHAn} - 2\text{e} \rightarrow 2(\text{AnCH}{=}\text{CHAn})^{+\bullet} \rightarrow {}^{+}\text{CH(An)CH(An)CH(An)(An)CH}^{+}$$

$$^{+}\text{CH(An)CH(An)CH(An)(An)CH}^{+} + 2\text{Nu}^{-} \rightarrow \text{NuCH(An)CH(An)CH(An)(An)CHNu}$$

where An = 4-MeOC_6H_4 and Nu = OH.



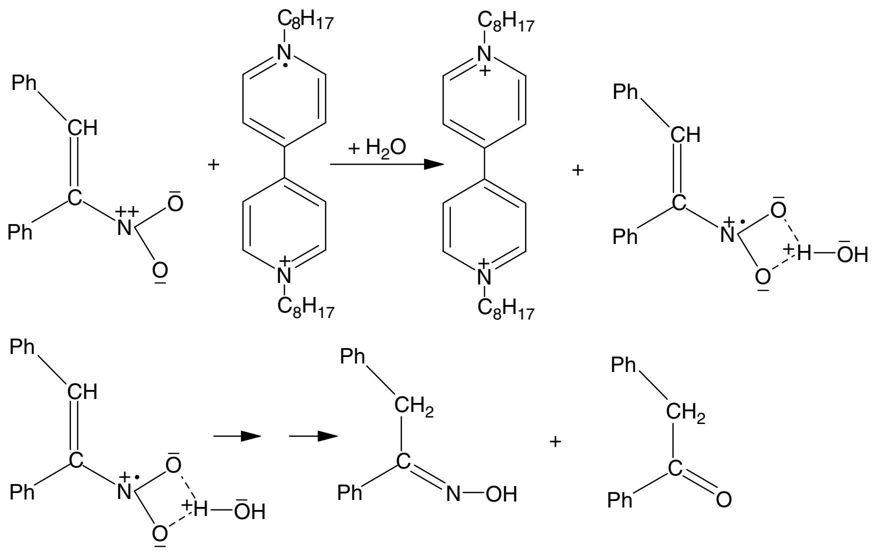
SCHEME 2.9

Another example concerns the initial electronic reduction of α-nitrostilbene (Todres et al. 1982, 1985, Todres and Tsvetkova 1987, Kraiya et al. 2004). The reduction develops according to direction a in Scheme 2.9 if the mercury cathode as well as cyclooctatetraene dianion are electron sources and according to direction b if the same stilbene enters the charge-transfer complexes with bis(pyridine)-tungsten tetra(carbonyl) or uranocene. For direction b, the charge-transfer bands in the electronic spectra are fixed. So the mentioned data reveal a great difference in electrochemical and chemical reduction processes a and b as they are marked in Scheme 2.9.

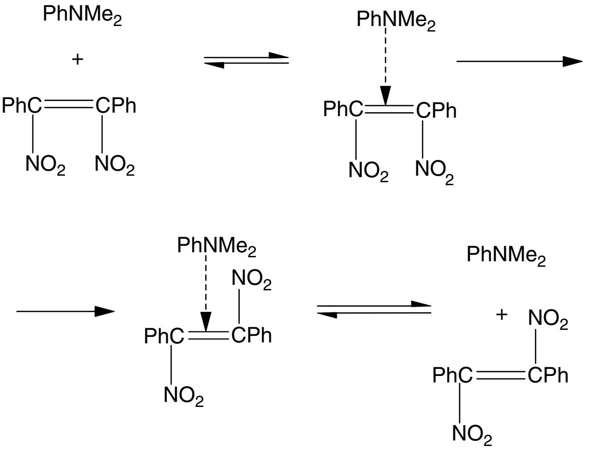
The difference between the two reactions of Scheme 2.9 may also be considered in terms of the complete electron transfer in both cases. If the α-nitrostilbene anion-radical and metallocomplex cation-radical are formed as short-lived intermediates, then the dimerization of the former becomes doubtful. The dimerization under electrochemical conditions may be a result of increased concentration of reactive anion-radicals near the electrode. This concentration is simply much higher in the electrochemical reaction because all of the stuff is being formed at the electrode, and therefore, there is more dimerization. Such a difference between electrode and chemical reactions should be kept in mind. In special experiments, only 2% of the anion-radical of α-nitrostilbene were prepared after interruption of controlled-potential electrolysis at a platinum gauze electrode. The kept potential was just past the cathodic peak. The electrolysis was performed in the well-stirred solution of *trans*-α-nitrostilbene in AN. Both processes developed in this case, namely, trans-to-cis conversion and dimerization (Kraiya et al. 2004). The partial electrolysis of α-nitrostilbene resulted in redox-catalyzed equilibration of the neutral isomers.

Interestingly, treatment of α-nitrostilbene in water–ethyl acetate mixture by the cation-radical of *N*,*N*′-dioctyl-4,4′-bipyridinium (the octylviologen cation radical) leads to the formation of products derived from the nitro group reduction. No dimerization is observed (Tomioka et al. 1986). Water is responsible for the fixation of transferred electron within the nitro group. Further reactions result in the formation of the corresponding oxime and ketone as shown in Scheme 2.10.

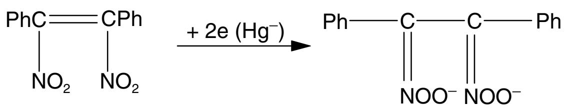
Being involved in a charge-transfer complex with *N*,*N*-dimethylaniline, *cis*-α,β-dinitrostilbene undergoes a conversion into its trans form with no changes in the nitro group (Todres et al. 1986; Scheme 2.11).



SCHEME 2.10

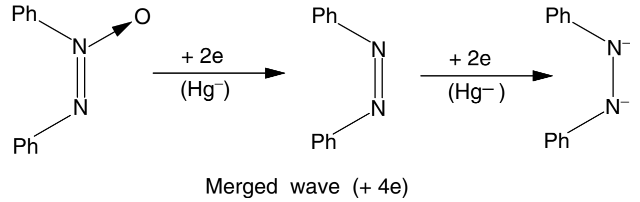


SCHEME 2.11

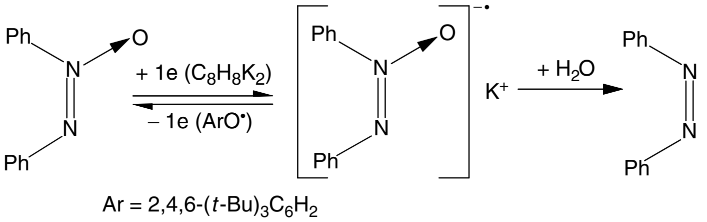


SCHEME 2.12

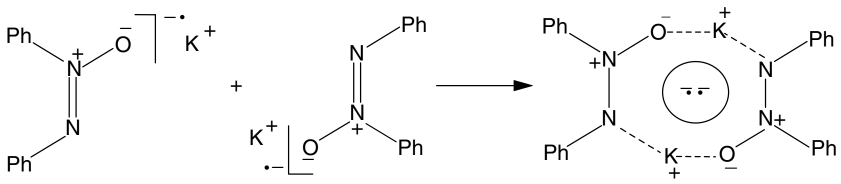
In contrast, one-electron polarographic reduction of α,β-dinitrostilbene yields an anion-radical, which is stabilized in a nitronic form with a carboradical center. These radicals possess an enhanced electron affinity and are prone to the capture of the second electron at the first wave potential, with the formation of a stable dinitronic dianion. In the case of α,β-dinitrostilbene, the cathodic reduction cannot be stopped at the one-electron step (Todres 1991; see Scheme 2.12).



SCHEME 2.13



SCHEME 2.14



SCHEME 2.15

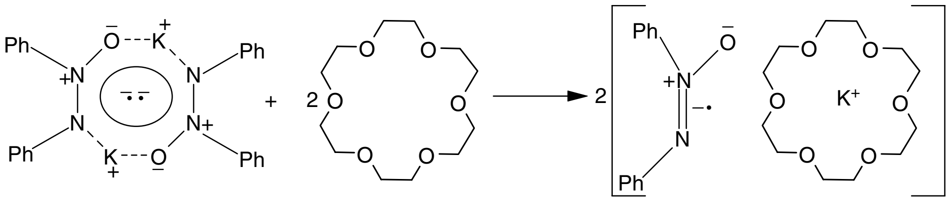
2.4.2 Template Effects

A similar situation occurs during electrochemical reduction of azoxybenzene. At the first polarographic wave, azoxybenzene forms azobenzene, which is more readily reduced than the initial substrate; the first and second waves are merged. In the absence of protons, a single polarogaphically irreversible four-electron wave is observed (see Scheme 2.13). Regardless of the nature of the supporting electrolyte (with cations of Bu_4N^+ or K^+), only a combined reduction process takes place (Lipsztain et al. 1974). For the reaction in Scheme 2.13, the azoxybenzene cis structure was chosen arbitrarily.

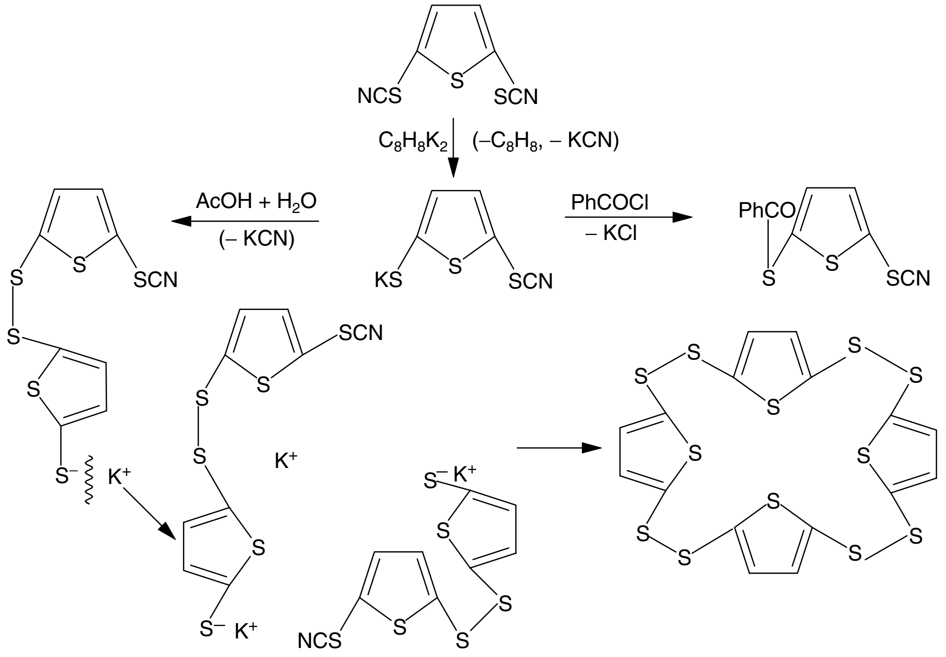
The behavior of the same azoxybenzene is studied in homogeneous conditions—when the dipotassium salt of cyclooctatetraene dianion ($C_8H_8K_2$) acts as a "dissolved electrode." In this case, the reduction of azoxybenzene stops at the very first stage, that is, after the transfer of one electron only (Todres et al. 1975). The initial one-electron reduction produces the azoxybenzene anion-radicals, which are not reduced further despite the presence of residual electron donor in the solution. The ESR method does not reveal these anion-radicals although one-electron oxidation by phenoxyl radicals quantitatively regenerates azoxybenzene and produces the corresponding potassium phenolate molecules in a quantitative yield. Treatment with water leads to a 100% yield of azobenzene (Scheme 2.14).

The logical conclusion reached while considering these data is as follows. In liquid phase (THF), under the conditions of a regular volume continuum without gradients of concentration and potential, all anion-radicals of azoxybenzene can be stabilized just after formation due to their bonding with potassium cations. This yields the coordinative complex. The complex is diamagnetic and, therefore, azoxybenzene anion-radicals cannot be revealed by ESR spectroscopy (Scheme 2.15).

The diamagnetic complex is not reduced further by the cyclooctatetraene dianion. This prevents the conversion of the azoxybenzene anion-radicals into azodianions. Potassium cation plays an important role in this limitation of the reduction process, which, generally, proceeds readily (the



SCHEME 2.16



SCHEME 2.17

electrode reduction takes place as a merged four-electron wave; see Scheme 2.13). It is very probable that potassium cations serve as bridges for the excessive electrons placing their low-lying orbitals at such π electron disposal. There are theoretical (Meccozi et al. 1996) and experimental (De Wall et al. 1999) proofs of potassium cation interaction with π electrons.

The removal of potassium cations from the reaction sphere can be accomplished by their binding with 18-crown-6-ether (Scheme 2.16).

The removal of potassium cations makes the results of the liquid-phase and electrode reactions similar. In the presence of crown ether, the eight-membered complex depicted in Scheme 2.16 is destroyed. The unprotected anion-radicals of azoxybenzene are further reduced by cyclooctatetraene dianion, losing oxygen and transforming into azodianion. The same particle is formed in the electrode reaction shown in Scheme 2.13. In the chemical reduction, stabilization of azodianion is reached by protonation. Namely, addition of sulfuric acid to the reaction results in the formation of hydrazobenzene, which instantly rearranges into benzidine (4,4′-diamino-1,1″-diphenyl). The latter was isolated from the reaction, which proceeded in the presence of crown ether.

2,5-Di(thiocyano)thiophene also presents a different behavior at a mercury-dropping electrode and in the case of treatment by dipotassium salt of cyclooctatetraene dianion; THF is the same solvent for both cases (Todres et al. 1979). The reaction between di(thiocyano) derivative and $C_8H_8K_2$ taken in equimolecular amounts leads to the formation of potassium salt of 2-mercapto-5-thiocyanothiophene (potassium mercaptide), potassium cyanide, and cyclooctatetraene (see Scheme 2.17). Potassium mer-

captide is stable in THF. It was characterized by a monobenzoyl derivative. If water is added to THF, a polysulfide is formed. X-ray analysis has unambiguously proved the cyclic structure of this polysulfide. The cyclization most probably proceeds via intermediate disulfides (see Scheme 2.17).

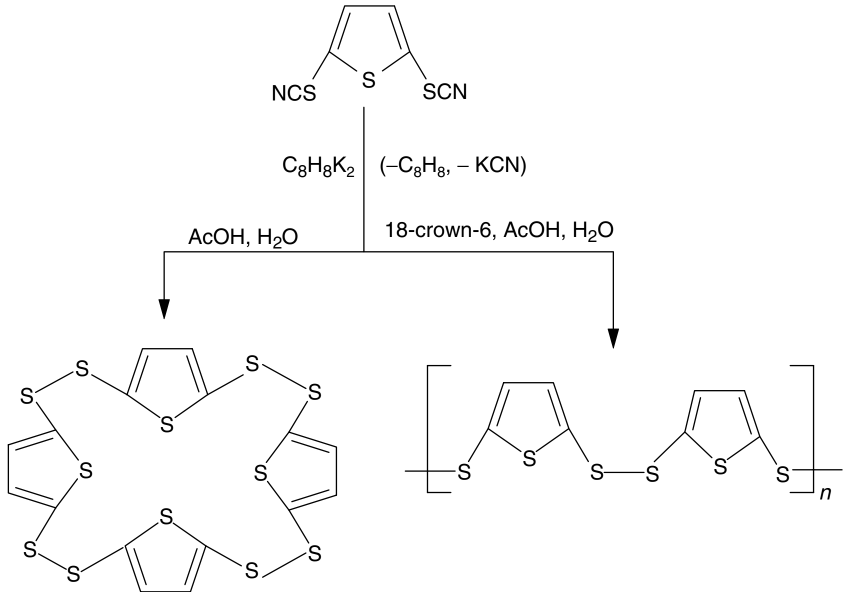
Again, the potassium cation acts as a coordination center, which ensures the template organization of anionic fragments during homogeneous reduction. The cavity diameter of the obtained multithiaheterocycle matches the doubled radius of potassium cation.

When 2,5-di(thiocyano)thiophene reacts with $C_8H_8K_2$ in the presence of 18-crown-6-ether, the other conditions being equal, the product formed was found to be a linear polysulfide. The crown ether encapsulates the potassium cation; the condensation changes its direction and leads to the formation of a linear product rather than a cyclic one (Scheme 2.18).

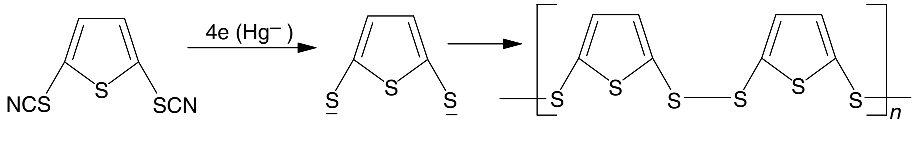
The linear product is obviously formed according to the sequence 2,5-di(thiocyano)thiophene → potassium 2-mercaptido-5-thiacyanonothiophene → tristhiomaleic anhydride ↔ thiophene-2,5-disulfenyl biradical (the diradical valence tautomer) → the depicted (Scheme 2.18) linear polymer in which the thiophene rings are connected by dusulfide bridges. It was recently confirmed that tristhiomaleic anhydride is unstable and polymerizes just at the moment of its formation (see Paulssen et al. 2000, Ref. 15 therein).

At a mercury electrode, 2,5-di(thiocyano)thiophene undergoes reduction, with the cleavage of both SCN groups within one four-electron wave. In the case of electrolysis, a linear polysufide can be obtained (Scheme 2.19).

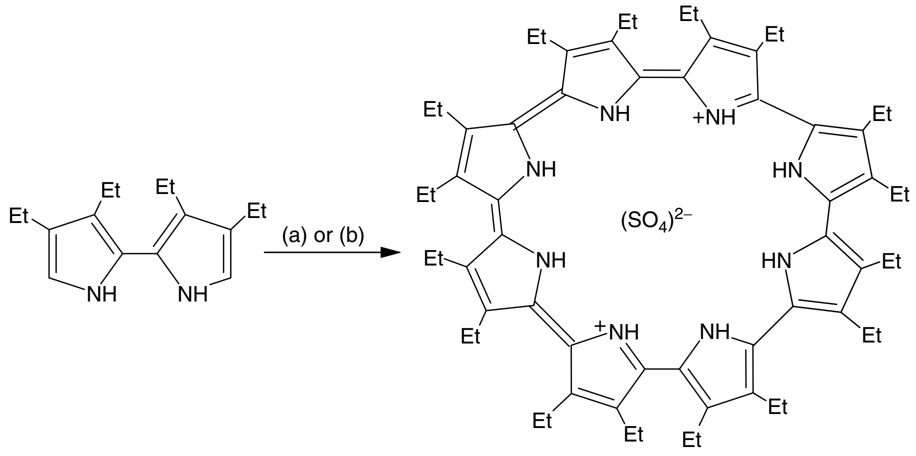
There is a case where the results of the electrode and chemical oxidation coincide (see Scheme 2.20). Calix[8]pyrrole was prepared from 3,3′,4,4′-tetraethyl-2,2′-bipyrrole during oxidative electrolysis in dichloromethane using platinum anode, tetrabutylammonium hydrogen sulfate as the



SCHEME 2.18



SCHEME 2.19



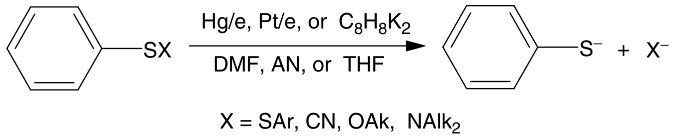
SCHEME 2.20

supporting electrolyte, and argon to provide an inert atmosphere (condition a in Scheme 2.20). The final product was obtained in the form of a dication and contained sulfate in the inner cavity (Bucher et al. 2006). The same cyclic structure was obtained by chemical synthesis when the starting tetraethylbipyrrole was treated with ferric chloride and sulfuric acid in dichloromethane (condition b in Scheme 2.20). The results of a single-crystal x-ray diffraction analysis showed that all four oxygen atoms of the sulfate counterion interact with all eight pyrrole NH sites in the center of the cycle formed. The sulfate anion is kept inside the cycle by electrostatic force and at the expense of hydrogen bonding. The sulfate anion, present in this structure, retains even when its solution in methylene chloride was washed by water three times (Seidel et al. 2002). The sulfate removal is only possible under repeated treatment by the phase-transfer catalyst Aliquat 336-nitrate in the toluene emulsion with aqueous sodium hydroxide solution. The free base (the octamethyl-octaundecylcyclo[8]pyrro le was tested) is an excellent extractant for wastes and displays a high selectivity for sulfate anion in the presence of excess nitrate (Eller et al. 2007).

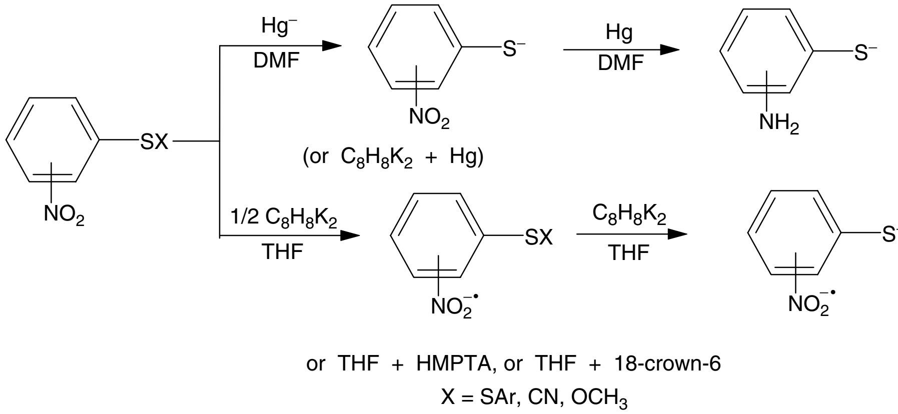
Both the reactions, anodic and chemical, proceed in a stepwise fashion and the bipyrrole cation-radicals are the key intermediates. The sulfate anion acts as a trigger in preorganizing the template synthesis depicted as in Scheme 2.20. Here sulfate plays the same role as potassium cation plays in the assembling of dithienyl disulfide in Scheme 2.17. Note that, in the absence of potassium cation, both the chemical and cathodic reductions lead to the formation of linear oligodisulfide although mechanisms of these reactions are obviously different. In particular, the exhaustive reduction of 2, 5-di(thiocyano)thiophene can be influenced by thiocyano-group affinity for mercury of the electrode. The waves observed, however, have diffusion characteristics. Thus, the cathodic process, although it is not connected with discrete formation of ion-radicals, has two interesting features. On one hand, it demonstrates the significance of the template effects on organic electron-transfer reactions proceeding under the conditions when participation of the alkali metal cation is possible. On the other, it suggests that just diffusion waves may, sometimes, reflect the reduction of depolarizers after their adsorption on electrodes. This phenomenon deserves a separate consideration because it is very unusual in organic electrochemistry. When compared to homogeneous electron-transfer reactions, such “hidden” adsorption inserts new colors in the general picture of ion-radical formation.

2.4.3 Adsorption Phenomena

In some cases, hidden adsorption is responsible for the differences between electrode and purely chemical redox reactions. The aromatic derivatives of divalent sulfur on reduction at the mercury-dropping electrode do not show any adsorption waves within the corresponding polarogam. Thus, the reduction



SCHEME 2.21



SCHEME 2.22

of derivatives of benzene sulfenic acid is independent of the nature of the electron donor and leads to phenylthiolate ion (Scheme 2.21; Todres 1980). These results were corroborated by later works with the use of glassy carbon electrodes and quantum-mechanical calculations (Kilimnik et al. 1982, Antonello et al. 2002, Baumgartner and Foray 2003, Houmam et al. 2003, Ji et al. 2004).

However, the analogs containing the nitro group exhibit different behavior in reactions at the surface of the electrode and on reduction by the cyclooctatetraene dianion. The difference is depicted in Scheme 2.22 (Todres 1980).

The addition of mercury in reaction mixtures of nitroarylsulfenates with $C_8H_8K_2$ in THF did not change the reaction results. Disintegration of the $XSC_6H_4NO_2^{-\bullet}K^+$ ion pairs (controlled through ESR method) does not affect the reaction results either. The polarographic reduction of the nitro derivatives proceeds with the primary cleavage of the sulfur-containing group (two-electron irreversible diffusion wave). The primary products of the homogeneous reaction are stable anion-radicals that can exist under air-free conditions for a long time. The cyclooctatetraene dianion, taken in excess, is capable of reducing the sulfur-containing group, too. However, the primary and detectable product of the homogeneous reaction is the anion-radical, which is not detected during reduction at the electrode. Electrochemical studies were carried out in aprotic solvents and no evidence for the adsorption of the sulfur-containing substances on the electrode was found. Only diffusion waves were observed.

The dissimilarity found between the homogeneous and heterogeneous reduction processes can be attributed to a specific interaction of the sulfur-containing groups with the material of the electrode.

Some literature sources supporting this point of view can be mentioned. The formation of asymmetrical dialkyl disulfide from two symmetrical ones is the well-known reaction: RSSR + R′SSR′ → 2RSSR′. This exchange is strongly accelerated by mercury metal (Hoffmann et al. 1999). Polarographic studies of diphenyl disulfide or methylphenyl sulfenate (Persson and Nygard 1974, Persson and Lindberg 1977) reveal that the interaction of these substances with mercury precedes the electron transfer in DMF. Namely, both PhS—SPh and PhSH are reduced together, in the framework of the same polarographic wave. It was also shown that $E_{1/2}$ values of the first wave of PhS—SPh and second wave of PhS—Hg—SPh coincide. Therefore, the formation of PhS—Hg—SPh or PhS—Hg—Hg—SPh can really precede the electron-transfer reaction from the mercury-dropping electrode to PhS—SPh.

There are other examples of organic thiocalomel formations during reduction by mercury cathodes (Reutov and Butin 1975, Giannakopoulos and Delgiannakis 2007). Lifetimes of dialkyl and diaryl thiocalomels do not exceed 10^{-2} and 10^{-4} s, respectively. The electrochemical activity of sulfur compounds at the mercury electrode is mainly defined by the interaction of the sulfur-containing groups with the electrode material rather than the redox transformation of the sulfur-containing groups themselves.

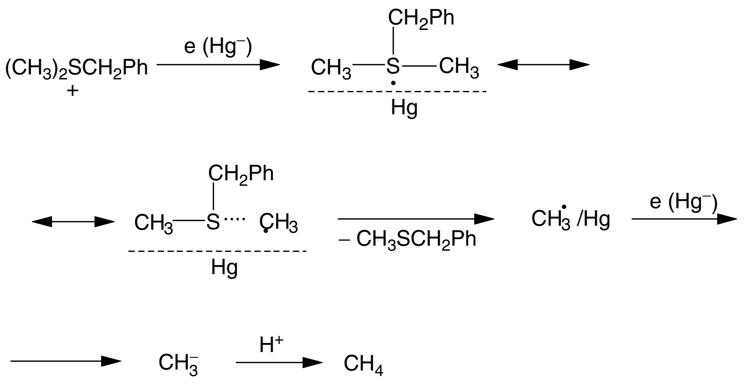
Hence, the reduction of arenesulfenates at the mercury electrode can proceed by the formation of intermediate arenethiomercuric derivatives. Such derivatives are reduced just after their formation and more easily than the initial arenesulfenates. In line with this argument, it logically follows that the limiting currents of the polarographic waves would depend solely on the diffusion of substances to the electrode. In fact, diffusion currents have been observed experimentally. Experiments of electrolysis on mercury (a preparative scale) confirmed the general conclusion (Todres 1988).

As an analogous example, the behavior of sulfonium salts can be mentioned. At mercury electrodes, sulfonium salts bearing trialkyl (Colichman and Love 1953) or triaryl (Matsuo 1958) fragments can be reduced, with the formation of sulfur-centered radicals. These radicals are adsorbed on the mercury surface. After this, carboradicals are eliminated. The carboradicals capture one more electron and transform into carbanions. This is the final stage of reduction. The mercury surface cooperates with both the successive one-electron steps (Scheme 2.23; Luettringhaus and Machatzke 1964). This scheme is important for the problem of hidden adsorption, but it cannot be generalized in terms of stepwise versus concerted mechanism of dissociative electron transfer. As shown, the reduction of some sulfonium salts does follow the stepwise mechanism, but others are reduced according to the concerted mechanism (Andrieux et al. 1994).

It is worthwhile to underline the selectivity of the carbon–sulfur bond splitting: The methyl group preferentially splits off, and in the case of $(CH_3)_2(PhCH_2)S^+Br^-$, the quantity of CH_4 formed is 10 times higher than that of $PhCH_3$ (Luettringhaus and Machatzke 1964). The affinity of radicals for mercury is well known, and small-sized radicals ($CH_3^\bullet$) must be adsorbed more strongly than large-sized radicals ($PhCH_2^\bullet$). Scheme 2.23 illustrates this peculiarity. In this scheme, the incipient radical is not exactly the one that is more steadfast ($PhCH_2^\bullet$–benzylic stabilization), but one that is more comfortably placed on the electrode surface (small-sized effect).

Generally, for chemical adsorption a significant overlap between substrate and electrode orbitals is needed, that is, a weak chemical bond has to be established. This implies that there must be an orientation effect, depending on the symmetry of orbitals involved, and the substrate molecule must be fairly close to the electrode surface.

To illustrate such a feature, let us compare the reactions of *N,N*-dimethylaniline cation-radicals with nucleophiles in their dependence on the manner of the one-electron oxidation of the parent molecule. Works by Kirchgessner et al. (2006), Weinberg and Reddy (1968), and Andreades and Zahnow (1969)



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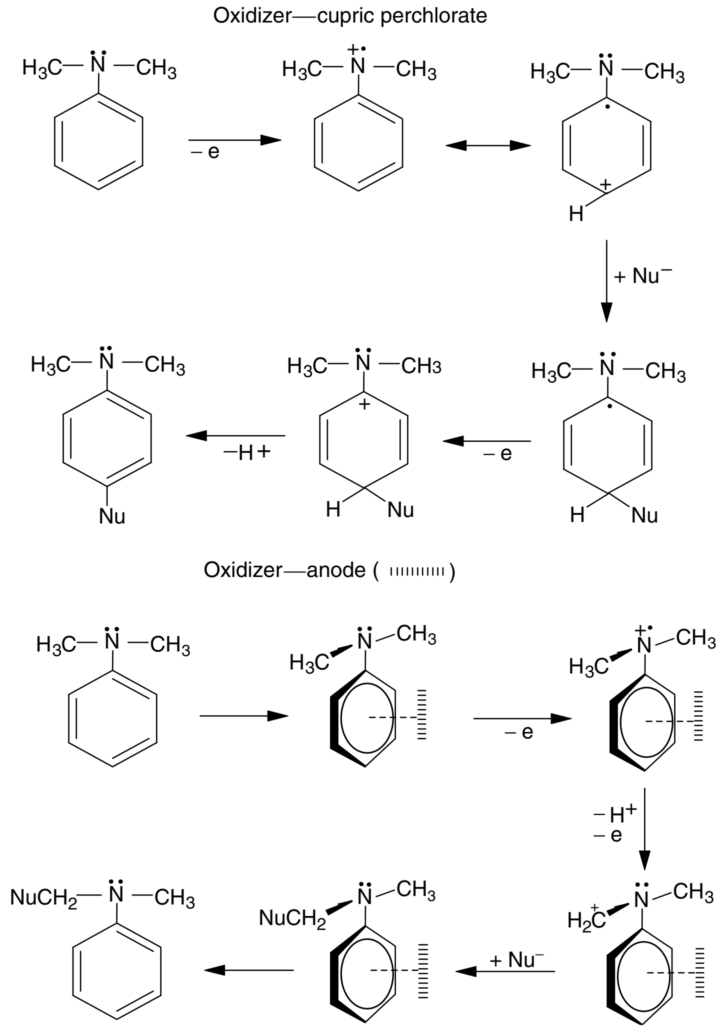
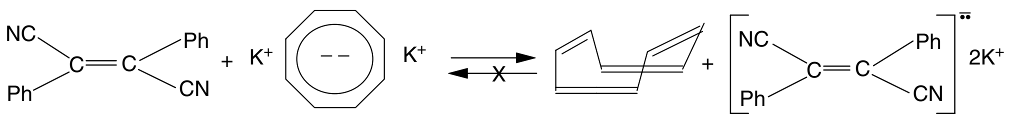


SCHEME 2.24

give a striking example of the difference between chemical and electrode oxidations of a substrate undergoing a further nucleophilic attack (Scheme 2.24). When the cation-radical of *N*,*N*-dimethylaniline was generated using cupric perchlorate as an oxidizer, the nucleophilic substitution proceeded into the para position of the phenyl ring (Kirchgessner et al. 2006; the top reaction in Scheme 2.24). When anode was used as an oxidizer, the nucleophilic substitution touched the methyl group, as per the formation of Ph–N(CH_3)CH_2^+ as the final product precursor (the bottom reaction in Scheme 2.24). This change in the orientation of the nucleophilic attack was explained by the strong adsorption of dimethylaniline and its cation-radical on the anode (Weinberg and Reddy 1968, Andreades and Zahnow 1969).

2.4.4 Stereochemical Phenomena

As mentioned earlier, an electrode reaction implies some orientation effect because a substrate molecule must be fairly close to the electrode surface. The following pairs of cis and trans isomers were reported to exhibit identical reduction potentials: 1,2-dimethyl-1,2-diphenylethylenes (Weinberg and Wienberg 1968); 1,2-bis(4-cyanophenyl)-1,2-bis(4-methoxyphenyl) ethylenes (Leigh and Arnold 1981); and 1,2-bis(4-acetylphenyl)-1,2-diphenylethylenes (Wolf et al. 1996).



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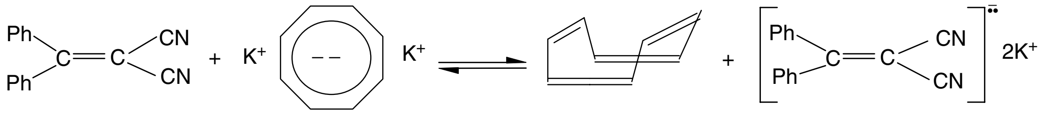


SCHEME 2.26

Particularly, the trans isomer of 1,2-dimethyl-1,2-diphenylethylene is coplanar and the cis isomer is noncoplanar. However, both isomers are oriented in an identical manner within the electrode space and electric field (Horner and Roder 1969). The energy needed for such an orientation is not markedly reflected in the value of a potential. For oxidation potentials, there are also data that these potentials are not sensitive to diastereoisomerism (Fukui et al. 2007).

Analogously, 1,2-dicyano-1,2-diphenylethylene, which is free from steric strains, and its strained isomer 1,1-dicyano-2,2-diphenylethylene are reduced at practically the same potentials (Ioffe et al. 1971, Todres and Bespalov 1972). In DMF, with the support of Et_4NI, the reversible two-step one-electron reductions are characterized by the following potentials (mercury pool as a reference electrode): −0.48 and −0.98 V for 1,2-dicyanoethylene and −0.50 and −1.07 V for 1,1-dicyano isomer. Thus, electrochemical reduction does not fix the difference in isomer structures.

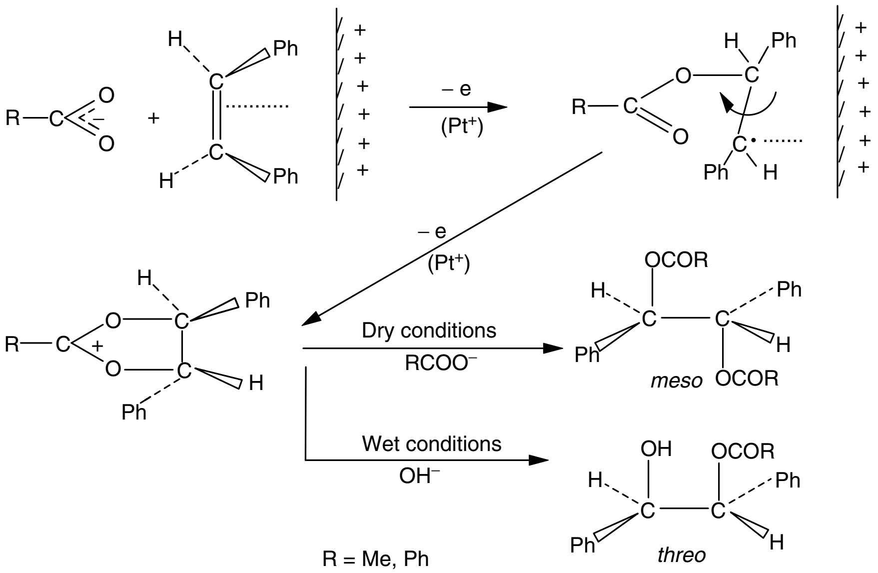
This difference is clearly displayed in homogeneous electron transfers (Ioffe et al. 1971, Todres and Bespalov 1972). When cyclooctatetraene dipotassium is used as an electron donor in a THF solution, the mentioned isomers react in an unlikely way. The 1,2-1,2-isomer takes the dianion's electrons off completely and irreversibly (Scheme 2.25).

On these same conditions, the reaction of 1,1-2,2-isomer is reversible (Scheme 2.26). With respect to the ethylene bond plane, the phenyl rings deviate only 30° in the 1,2-1,2-isomer and 90° in 1,1-2,2-isomer (Wallwork 1961, Todres and Bespalov 1972).

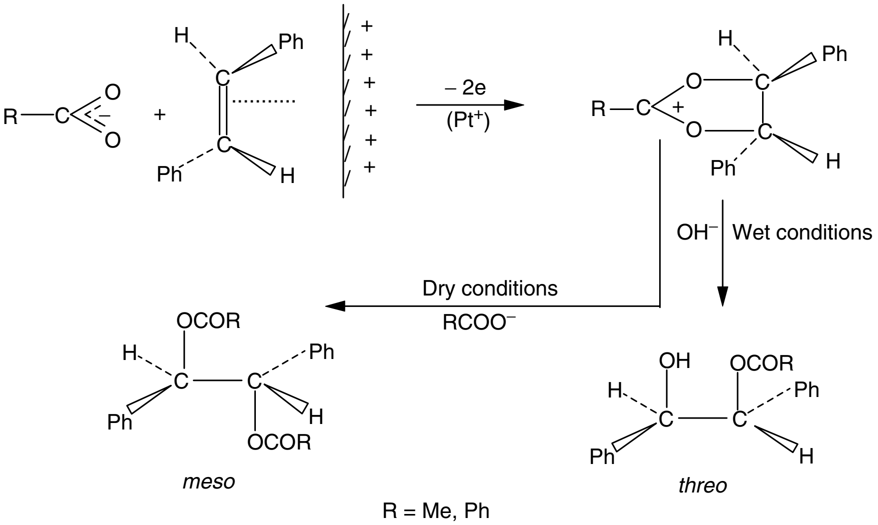
The conjugation chain includes all the structural elements in the 1,2-1,2-isomer. In the 1,1-2, 2-isomer, at least one of the phenyl groups is led out of the conjugation. According to calculations (Todres and Bespalov 1972), the aforementioned difference in bend angles is supposed to be the same in the corresponding dianions. Therefore, such an explanation of the reversibility for the 1,1-2, 2-isomer is reasonable. Because of steric hindrances in the geminal node, the conjugation chain is broken (is shortened). It leads to some diminution in the delocalization degree for an excess electron. This means that the stability of the electron-transfer product decreases. The electron-transfer reaction becomes less favorable and the transformation degree declines. This steric hindrance is tangible in other reductive transformations of 1,1-dicyano-2,2-diphenylethylene (see, e.g., the work by Tarnopolsky and Hoz 2007).

In summary, the space strain is indicative of the stability of electron-transfer products. Electrode reactions fail to reveal such an effect. In liquid-phase processes, this effect, however, plays a decisive role. As Baizer and Lund's book (1983, p. 907) underlines

> When the stereochemistry of an electrochemical reaction is discussed it is normally assumed that the geometry of the molecule in question remains essentially unchanged until bond breaking or bond transformation occurs. It should be recognized, however, that an electron transfer might entail significant changes in the geometry and bond strengths of a molecule with concomitant implications for the stereochemisty of its reaction (Todres 1974). Unfortunately, this important area has not been extensively investigated.

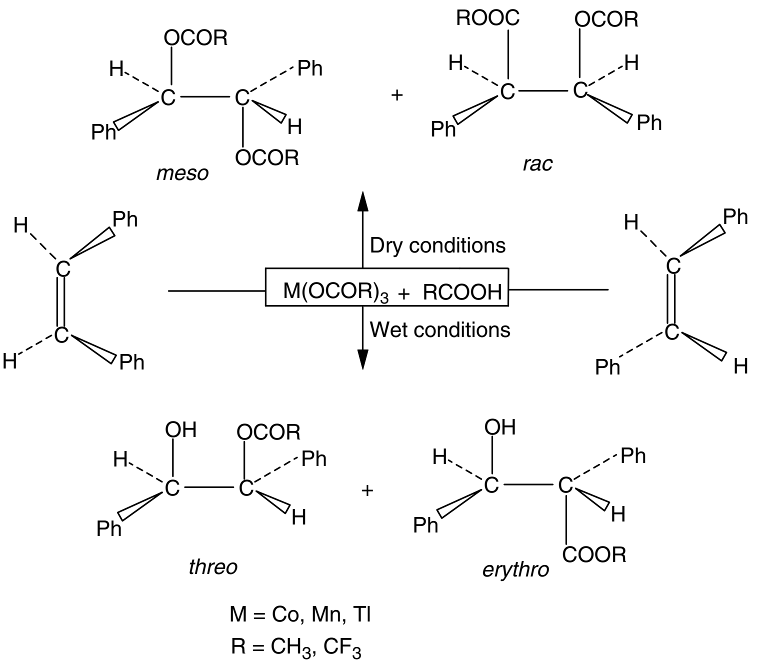


SCHEME 2.27



SCHEME 2.28

From this point of view, a brief comparison of acyloxylation of *cis*- or *trans*-stilbenes in electrochemical and chemical conditions is also relevant. Oxidation of *cis*- or *trans*-stilbene at the platinum anode in the presence of acetic or benzoic acid gives predominantly *meso*-diacylates of hydroxybenzoin or, if some water is present, *threo*-monoacylate. None of the stereoisomeric *erythro*-monoacylate and *rac*-diacylate were obtained in either case. There was no evidence of isomerization of *cis*- to *trans*-stilbene under the electrolytic conditions employed (Mango and Bonner 1964, Koyama et al. 1969). The sequence of reaction steps in Scheme 2.27 was proposed. Adsorption-controlled one-electron oxidation of the substrate takes place. Then the cis-stilbene cation-radical interact with acetate to form an oxonium ion. The phenyl groups in the oxonium adopt the trans mutual disposition which is thermodynamically preferential. The *trans*-benzoxonium ion is the common intermediate for conversions of both *cis*- and *trans*-stilbenes and, of course, for all the final products (Scheme



SCHEME 2.29

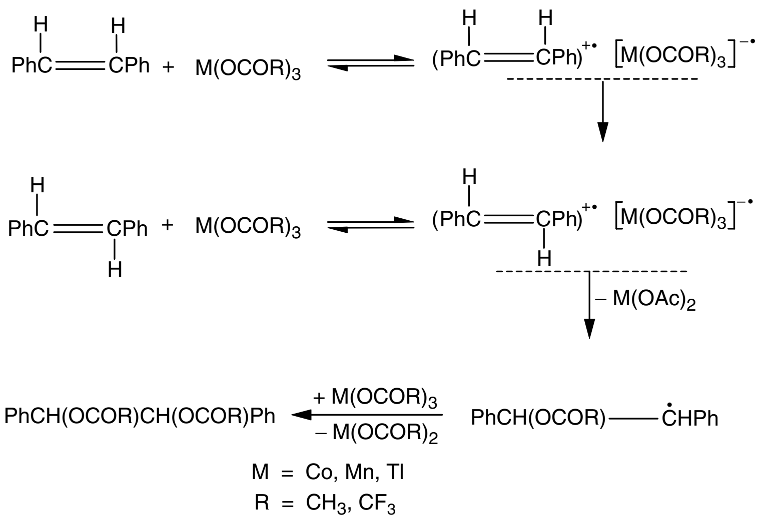
2.28). There are no passing into the solution volume, with the following electron being exchanged there with nonoxidized molecules of stilbene.

The chemical oxidation of *cis*- or *trans*-stilbene was also investigated (Vinogradov et al. 1976). The oxidant was cobalt or manganese acetate and, in separate experiments, thallium trifluoroacetate. Acetic or trifluoroacetic acid was used as a solvent. The results of such chemical oxidation were considered from the geometrical standpoint of the recovered (nonreacted) part of the initial substrate and stereoisomeric composition of the products obtained. This allowed the desirable comparison of electrochemical and chemical reactions to be made.

The cation-radicals of stilbene have been detected by ESR spectroscopy. These cation-radicals are accumulated and then consumed in the course of consecutive reactions. The stereoisomeric composition of the final products occurs to be constant and does not depend on the configuration of the initial substrate. Acetoxylation of the olefinic bond in *cis*-stilbene is almost one order of magnitude slower than in *trans*-stilbene. This kinetic feature deserves a special explanation, because *cis*-stilbene is less stable thermodynamically than *trans*-stilbene and should react faster. The products obtained are depicted in Scheme 2.29.

When the initial compound was *trans*-stilbene, the unconsummated part was recovered with no change in configuration. When *cis*-stilbene was employed as the initial reactant, the recovered olefin was a mixture of trans and cis isomers. Hence, the trans configuration is more favorable for oxidative acetoxylation than the cis configuration. In accordance with this conclusion, the mechanism shown in Scheme 2.30 is proposed.

It is seen that the cation-radical of stilbene, but not stilbene itself, is subjected to acetoxylation. Stilbene in trans form yields the trans form of the cation-radical, which undergoes further reaction directly. Stilbene in cis form gives the cation-radical with cis structure. The cis cation-radical at first acquires the trans configuration and only after this adds the acetate ion. It is the isomerization that causes the observed retardation of the total reaction. It is the absence of adsorption at the electrode surface that allows the nonacetoxylated part of *cis*-stilbene to isomerize and turn into the



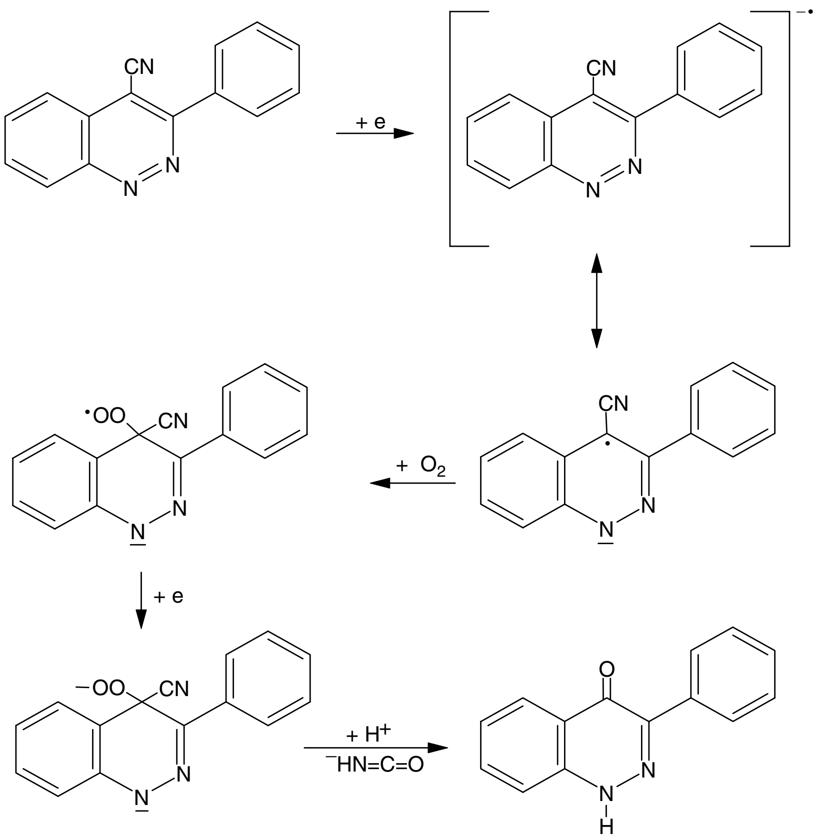
SCHEME 2.30

more rich stereoisomeric set of final products. To support this point of view, one can mention the cation-radical epoxidation, cylopropanation, and cycloaddition (Diels–Alder reaction) of stilbenes. Particularly, stereochemistry of the Diels–Alder reaction is complicated by competing cis to trans isomerization of the stilbene cation-radical (Yueh and Bauld 1995, 1996). In the reactions catalyzed with ammoniumyl ion, *cis*-stilbenes react approximately 2.5 times slower than *trans*-stilbenes, whereas in electrode oxidations the cis isomers are more reactive (Kim et al. 1993, Bauld and Yeuh 1994, Mirafzal et al. 1998, Adamo et al. 2000).

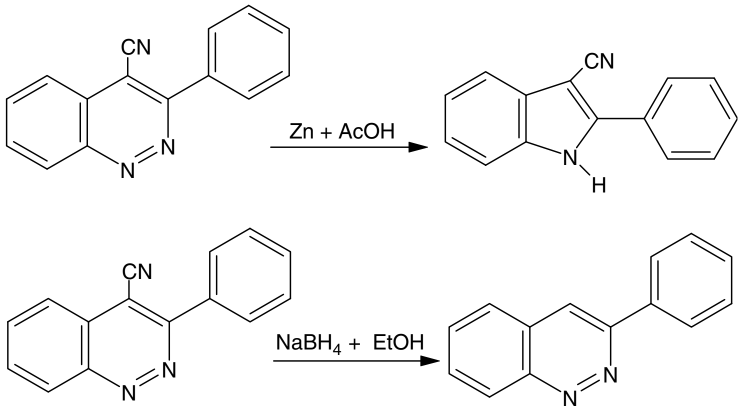
2.4.5 Concentration Effects on the Fate of Ion-Radicals at Electrodes and in Solutions

One disadvantage of the electrochemical reactions is the very high concentration of products at the electrode surface. This affects the ion-radical reactivity. To illustrate, let us compare chemical and electrochemical reductions of 4-cyano-3-phenylcinnoline in the presence of oxygen (Matsubara et al. 2000). Electrolysis of 4-cyano-3-phenylcinnoline (platinum cathode, potential [−8 V], benzonitrile solvent, tetrabutylammonium tetrafluoroborate electrolyte) was performed at room temperature in the presence of oxygen. Scheme 2.31 represents this electrode reaction including the mechanism proposed by Matsubara et al. (2000). The primary formation of 4-cyano-3-phenylcinnoline anion-radical was reliably established. In the near-electrode space, the anion-radical is just intercepted by oxygen. Naturally, oxygen adds to the position of maximal spin density. This leads to the elimination of isocyanic acid so that the reaction eventually gives rise to 3-phenyl-4(1H)-cinnolone in 100% yield. The electrochemical transformation of 4-cyano-3-phenylcinnoline into 3-phenyl-4(1H)-cinnolone proceeds efficiently under mild conditions and is applicable to diverse 3-phenyl derivatives (Matsubara et al. 2000). This reaction can be used as a method of cinnolone electrochemical synthesis.

The chemical reduction of the same 4-cyano-3-phenylcinnoline in the presence of oxygen in air leads to quite different products when compared to the electrode process. The reactions were carried out in a dilute solution in which the chemicals were evenly distributed. On action of zinc dust in acetic acid at 25°C, the parent compound gives 3-cyano-2-phenylindole in quantitative yield. Reaction of the same starting material with sodium borohydride in ethanol under reflux provides 3-phenylcinnoline at almost quantitative yields (Matsubara et al. 2000, Ref. 13). The products mentioned are depicted in Scheme 2.32.



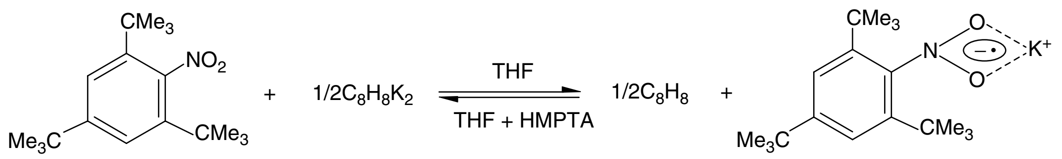
SCHEME 2.31



SCHEME 2.32

2.4.6 Aggregation of Ion-Radical Salts

Organic ion-radicals bear charges that must be compensated. In solutions, the ion-radicals exist in the form of salts. Under certain conditions, interaction between the counterions of the salt can be very strong forming the so-called ion pairs. An ion pair consists of two oppositely charged ions that held together by attraction between the unlike charges. Ion-pair formation defines the energies of an ion-radical salt and, consequently, the energy of a reaction that leads to ion-radical formation.



SCHEME 2.33

To study the role of ion pairs, it is necessary to investigate electron-transfer reversibility in a solution and compare the results obtained with redox potentials of a donor and an acceptor. As a rule, ion-pairing phenomena define electrode processes too (Baizer and Lund 1983). However, the known equations for equilibrium calculations cannot take ion pairing into consideration because the equations do not contain ion-pair terms. One has to rely on experiments, which are able to take into account the equilibrium of electron transfer in solutions.

2.4.6.1 Direct Influence on Electron-Transfer Equilibrium

The reaction between cyclooctatetraene dipotassium and 2,4,6-tri(*tert*-butyl)nitrobenzene in THF is irreversible. The acceptor gives rise to an anion-radical salt. An unpaired electron of the organic anion-radical is predominantly localized within the nitro group. The potassium cation is coordinated with the anion-radical nitro group. Such coordination also enhances this localization. Thus, the reaction leads to a very stable species, which is unable to reverse one-electron transfer to cyclooctatetraene. Being a very strong dissociating solvent, hexamethyl phosphotriamide (HMPA) destroys the K^+ coordination complex with $ArNO_2^{-\bullet}$, and the reaction becomes reversible (Todres 1970, 1980; Scheme 2.33).

Now let us focus on an important group of ion-radical reactions, that is, recombinations. They may proceed as either disproportionation or dimerization. It is interesting to compare the ion-radical and *uncharged* radical recombination. As known, the uncharged radicals recombine at zero activation energy. Ion-radicals have a dual nature—as radicals they are highly reactive, and as ions they attract particles of an opposite charge and repel those of the same charge. Disproportionation is the interaction between ion-radicals of equal signs. It depends on two factors, namely, charge-repulsion- and spin-pairing energy. A decrease in charge-repulsion energy, naturally, promotes recombination. This energy is large, when naked ions react. This energy decreases significantly when tight pairs with counterions are involved.

Understandably, the stability of ion pairs depends on the nature of a solvent, particularly on its dissociating ability. For example, in HMPA (a strong dissociating solvent), the potassium salt of tetraphenylethylene anion-radical disintegrates. In THF (a nondissociating solvent), ion pairs $(Ph_2C{=}CPh_2)^{2-}$, $2K^+$ or $(Ph_2C{=}CPh_2)^{-\bullet}$, K^+ are stable (Czezhegyi et al. 1969). The most important effect of this aggregation between the counterions consists of diminution of the resulting negative charge of anion-radicals. In other words, electrostatic repulsion between these anion-radicals is decreasing. This favors the recombination of anion-radicals. Therefore, in THF $(Ph_2C{=}CPh_2)^{-\bullet}$, K^+ disproportionates rapidly. In HMPA, naked $(Ph_2C{=}CPh_2)^{-\bullet}$anion-radical exists for a long time and the disproportionation equilibrium is strongly shifted to the left (Todres 1985) as follows:

$$[Ph_2C{=}CPh_2^{-\bullet}, K^+]\cdot THF + [Ph_2C{=}CPh_2^{-\bullet}, K^+]\cdot THF \rightleftharpoons Ph_2C{=}CPh_2$$
$$+ [Ph_2C{=}CPh_2^{2-}, 2K^+]\cdot THF$$

Hence, a very important factor of preferential dianion formation is the decrease in electrostatic repulsion between anion-radicals. By changing the ion-pair stability, particularly, by solvent selection, one can manage the equilibrium of liquid-phase electron-transfer reactions.

A special case of disproportionation as a consequence of ion association is mentioned in conclusion. If a suspension of triethyloxonium hexachlorantimonate and tetrakis(anisyl)ethylene,

$An_2C{=}CAn_2$, is stirred in dichloromethane, their corresponding cation-radical salt forms quantitatively (Rathore et al. 1998):

$$2An_2C{=}CAn_2 + 3Et_3OSbCl_6 \rightarrow 2(An_2C{=}CAn_2)^{+\bullet}SbCl_6^- + 3EtCl + 3Et_2O + SbCl_3$$

Slow crystallization of salt from the reaction solution layered with diethyl ether leads to the formation of a mixture of tetrakis(anisyl)ethylene cation-radical and dicationic salts along with tetrakis(anisyl)ethylene. All the compounds precipitate from the solution containing the cation-radical salt only. The formation of dication is a result of disproportionation.

$$2(An_2C{=}CAn_2)^{+\bullet}SbCl_6^- \rightarrow (An_2C{=}CAn_2)^{2+}(SbCl_6^-)_2 + An_2C{=}CAn_2$$

Hence, two possible causes of this disproportionation should be taken into account—changes in the solution parameters during slow mixing of the solvent layers (dichloromethane and diethyl ether) and requirements with respect to the closest packing in crystals.

2.4.6.2 Electron-Transfer Reactions with Participation of Ion-Radical Aggregates

The disodium salt of diphenylacetylene dianion is stable in THF solution at −78°C. Methanol acts as a proton source toward the salt and causes the formation of a mixture of 1,2-diphenylethane with diphenylacetylene and small amounts of *trans*-stilbene (Chang and Johnson 1965, 1966). It seems logical that the reaction between $(PhC{\equiv}CPh)^{2-}$, $2Na^+$ and MeOH leads at first to PhCH=CHPh. The second step is supposed to consist of the further reduction of PhCH=CHPh at the expense of electrons from the nonreacted part of the initial dianion. In principle, the electron transfer may proceed faster than the reaction of the initial dianion with protons. As a result, the diphenylacetylene dianion has to discharge into diphenylacetylene, whereas stilbene dianion has to form diphenylethane as follows:

$$(PhC{\equiv}CPh)^{2-}, 2Na^+ + PhCH{=}CHPh \rightarrow PhC{\equiv}CPh + (PhCH{=}CHPh)^{2-}, 2Na^+$$

$$(PhCH{=}CHPh)^{2-}, 2Na^+ + 2MeOH \rightarrow 2MeONa + PhCH_2CH_2Ph$$

Hence, one could predict that being mixed with methanol, the solution of PhCH=CHPh, $(PhC{\equiv}CPh)^{2-}$, $2Na^+$ in THF might give $PhCH_2CH_2Ph$ and PhC≡CPh in quantitative yields.

This obvious supposition occured to be false—the addition of stilbene causes no changes in the results of the reaction (Chang and Johnson 1965, 1966). It follows that an effective contact between PhCH=CHPh and $(PhC{\equiv}CPh)^{2-}$, $2Na^+$ is less than probable. As known, $(PhC{\equiv}CPh)^{2-}$, $2Na^+$ is a polymeric aggregate $[(PhC{\equiv}CPh)^{2-}, 2Na^+]_n$. Bulk stilbene molecules are incapable of diffusing inside the aggregate. At the same time, the penetration of proton (or methanol) seems to be possible.

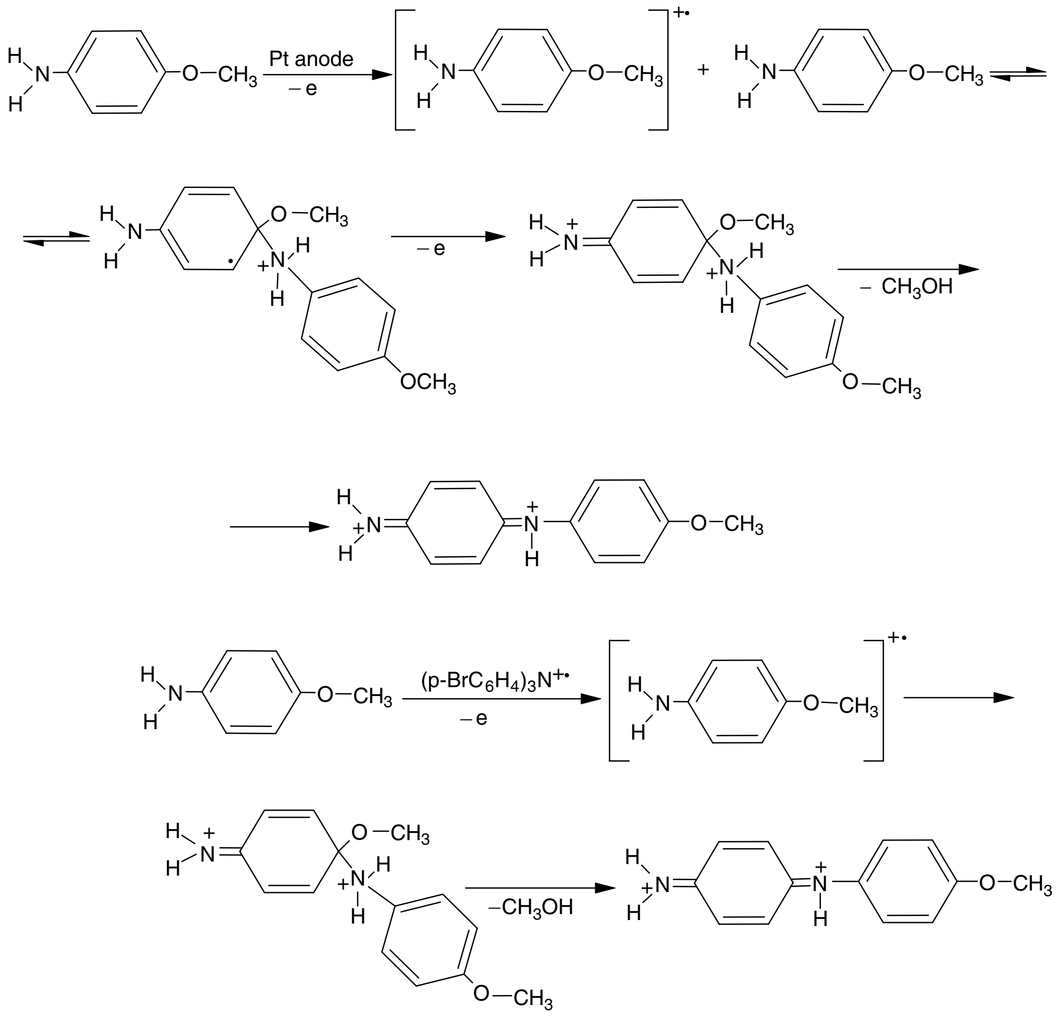
Here, it would be interesting to explore the behavior of acetylenic cation-radicals. Studies of negative Fukui functions for a family of substituted acetylenes showed that removing an electron from the HOMO induces electron rearrangement so that the electron density along the carbon–carbon bond increases. In other words, the electron density in one region of the molecule increases although the total number of electrons decreases (Melin et al. 2007). It must reflect in the reactivity of the acetylenic cation-radicals.

$(PhCH{=}CHPh)^{2-}$, $2Na^+$ also seems to be capable of existing in the polymeric form in the THF solution. This salt is a typical initiator of polymerization of unsaturated compounds such as isoprene or methylstyrene. In THF, such polymerization can include a detachment or fixation (chemisorption) of a framing (terminal) link from the polymeric aggregate $[(PhCH{=}CHPh)^{2-}, 2Na^+]_n$. Methylstyrene captures the "come-off" link, starting the polymerization process. The link and, probably, $[(PhCH{=}CHPh)^{2-}, 2Na^+]_{n-1}$ oligomer are included in a polymeric globule. The situation resembles a snake in a cage. In experiments (Podol'sky et al. 1982), α-methylstyrene was polymerized in THF by the action of $[(PhCH{=}CHPh)^{2-}, 2Na^+]_n$ labeled with ^3H and ^{14}C in the presence of nonlabeled PhCH=CHPh. The authors obtained a polymer that contains the whole amount of the label. In case of the mixture of nonlabeled $[(PhCH{=}CHPh)^{2-}, 2Na^+]_n$ with labeled PhCH=CHPh in THF, the polymer obtained did not contain any label.

These chemical electron-transfer reactions are in contrast with the electrode reactions. For instance, stilbene gives a mixture of 1,2-diphenylethylene with 1,2,3,4-tetraphenylbutane on electrolysis (Hg) in DMF at potentials about that of the first one-electron wave. This solvent has faint proton-donor properties. The stilbene anion-radical is stable under these conditions; it has enough time to diffuse from the electrode into the solvent and dimerize therein (Wawzonek et al. 1965).

2.4.6.3 Kinetic and Mechanistic Differences between Electrode and Chemical (Homogeneous) Ion-Radical Dimerization

Goto et al. (2004) measured the reaction kinetics of one-electron oxidation of *N*-methyl-*p*-anisidine in AN. In the electrode process, oxidation was performed at the platinum disk-shaped anode, in the chemical process, by means of the tris(*p*-bromophenyl)amine cation-radical. In both the cases, after one-electron oxidation, dimerization took place leading to the formation of the dye variamine blue. According to the kinetic data, the mechanism of this dye formation is different in the electrode and chemical processes (see Scheme 2.34). Namely, in the electrode oxidation, the cation-radical appears to be surrounded by a huge amount of the initial (nonoxidized) *N*-methyl-*p*-anisidine



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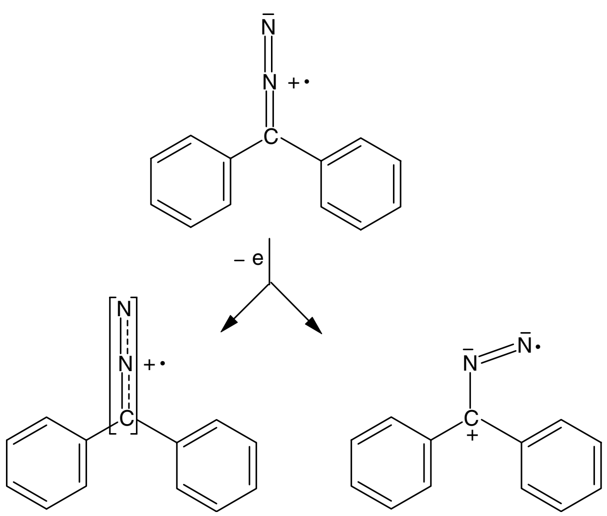


SCHEME 2.35

molecules. Therefore, dimerization proceeds with the participation of the charged and neutral species. In the homogeneous process, all the *N*-methyl-*p*-anisidine species are present in cation-radical forms. Therefore, dimerization proceeds as a coupling of two cation-radicals. This difference in the mechanisms reflects in the reaction kinetics.

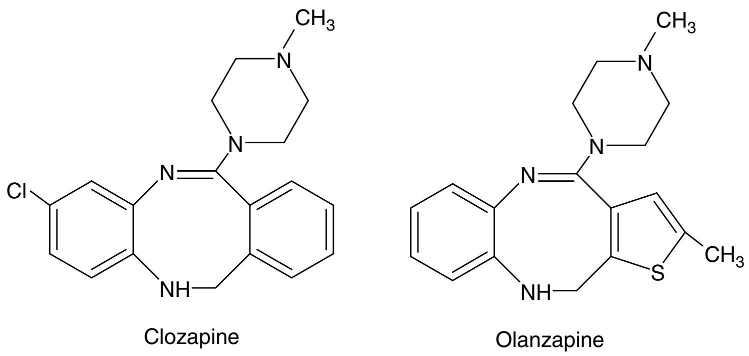
The phenomena enumerated in Section 2.4 do not, of course, fully describe all the differences and similarities between chemical and electrode processes of ion-radical formation. From time to time, effects that cannot be clearly interpreted and categorized are found. For example, see the paper titled "π- and σ-Diazo Radical Cations: Electronic and Molecular Structure of a Chemical Chameleon" (Bally et al. 1999). In this work, diph enyldiazomethane and its $^{15}N_2$, ^{13}C, and D_{10} isotopomers were ionized through one-electron electrolytic or chemical oxidations. Both reactions were performed in the same solvent (dichloromethane). Tetra-*n*-butylammonium tetrafluoroborate served as the supporting salt in electrolysis. The chemical oxidation was carried out with tris(4-bromophenyl)- or tris(2,4-dibromophenyl)ammoniumyl hexachloroantimonate. Two distinct cation-radicals that corresponded to π and σ types were observed in both the processes of one-electron oxidation (see Scheme 2.35). The electromers differ drastically in their optical and ESR spectra. There is a rather small energy difference between them (ca. 1 eV).

The authors conclude that "the experimentally found energetic proximity of the two states is not an intrinsic property of the diaryldiazo cation-radicals, but must be due to some solvent or counterion effects acting to preferentially stabilize the σ state by about 1 eV." These effects, however, failed to be identified in the quoted paper. Further development of the problem remains to be seen.

2.5 FORMATION OF ORGANIC ION-RADICALS IN LIVING ORGANISMS

One-electron transfer reactions are typical in living organisms. Ion-radicals are acting participants of metabolism. Of course, such ion-radicals are instantly included in further biotransformations. Therefore, it is reasonable to consider the problem of ion-radical formation together with the data on their behavior in biosystems. Chapter 3 contains a special section covering this topic. However, the issue of competition for an electron during ion-radical formation deserves to be mentioned here.

Sometimes, mesonidazole and AF-2 medication are administered jointly. Mesinidazole is 1-(2-nitroimidazol-1-yl)-3-methoxypropan-2-ol and AF-2 is 2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide. It is clear that the latter is a stronger acceptor than the former. When anion-radicals of mesonidazole are formed, they pass their unpaired electrons to molecules of AF-2. One medicament cancels the action of the other (Clarke et al. 1984a,b).



SCHEME 2.36

Ion-radical generation is a result of the interaction between some organic species and enzymes or other participants of metabolism. First, we should note that the so-called cell conditions can determine the very possibility of electron transfer. For example, there is a well-founded assumption that the reduction potential of colchicine is lowered enough on contact with proteins, particularly in tumor cells, to accept an electron (Cavazza et al. 1999). The cell conditions can also determine whether an enzyme acts as an oxidative- or a reductive agent. Cytochrome P450 enzymes are hemoproteins of significant importance in the oxidation of a wide variety of drugs, pesticides, carcinogens, steroids, and fat-soluble vitamins. They contain an Fe^{3+} center, which transforms into an Fe^{2+} kernel. These enzymes are well-known biological oxidants. However, they can also catalyze reduction, cycling between Fe^{2+} and Fe^{3+} forms.

Clozapine and olanzapine are atypical antipsychotic drugs used in the treatment of schizophrenia. Their structures are depicted in Scheme 2.36. The use of clozapine and olanzapine, which are more effective than standard neuroleptic drugs in the treatment of refractory schizophrenia, is, however, limited because of their adverse effects. These adverse effects are ascribed to the formation of the corresponding cation-radicals in living organisms under oxidation by bone marrow cells. These cation-radicals eliminate protons from the NH fragments and generate their nitrenium cations. The nitrenium cations are covalently bound to the life-important proteins. This results in the toxic effects of clozapine and olanzapine (Sikora et al. 2007).

Combination of phenol(thiol)-type antioxidants with the drugs of the phenothiazine group leads to synergism in fighting against Chagas disease (see a review by Gutierrez-Correa 2006) with the symbolic title "*Trypanosoma cruzi* dihydrolipoamide dehydrogenase as target for phenothiazine cationic radicals. Effect of antioxidants." The Chagas disease is widely prevalent in the American hemisphere from southern United States to southern Argentina. It is endemic in 21 countries, with 18–20 million persons infected and 40 million people at risk of acquiring the disease. The disease is transmitted into humans by hematophagous *Reduviid* insects and also directly by transfusion of infected blood. From the insects, trypomastigotes are introduced through abraded skin at the site of biting. The trypomastigotes penetrate into the human cells, rupture them, emerge from the ruptured ones, reach adjacent cells and bloodstream, and spread within the organism. The acute phase of the disease is usually seen in children and is characterized by fever, malaise, anorexia, adenopathy, or local sign of inflammation at the site of the insect bite. However, generally, there is no clear acute stage and persons infected may remain free of symptoms. In about one-third of acute cases, a chronic form develops approximately 10–20 years later, causing cardiomyopathy or gastrointestinal dysfunction. Patients with chronic disease die usually from heart failure. Recent studies indicate that there are ca. 200,000 new infected cases and 21,000 deaths by Chagas disease every year (Urbina and Docampo 2003). At present, there is no effective treatment for such patients.

The drugs most frequently used in the treatment of Chagas disease are nifurtimox and benznidazole. But both of them have very low antiparasitic activity in the chronic stage of the disease and

bring serious side effects. The Gutierrez-Correa's (2006) review summarizes recent results testifying for the high efficiency of the phenothiazine drugs in the treatment of patients. In particular, promazine, trimeprazine, and thioridazine are recommended. Their efficiency is caused by the ease in which the cation-radicals are formed on oxidation by myeloperoxidase, myoglobin, and peroxidase. The transient formation of these cation-radicals was confirmed by ESR and optical spectroscopy. The species irreversibly block the active principle of Chagas disease (*Trypanosoma cruzi* dihydrolipoamide dehydrogenase). In the pres ence of phenol (thiol) antioxidants, phenothiazine cation-radicals play another role—on reacting easily with antioxidants, they are suppressed. But the cation-radical quenching generates radicals in the physiological system. These radicals show enhanced cytotoxicity. Combined administration of phenothiazins and antioxidants brings about an enhanced therapeutic effect, smoothed in terms of side effects.

Electron-transfer chains in plants differ in several striking aspects from their mammalian counterparts. Plant mitochondria are well known to contain alternative oxidase that couples oxidation of hydroquinones (e.g., ubiquinol) directly to reduction of oxygen. Semiquinones (anion-radicals) and superoxide ions are formed in such reactions. The alternative oxidase thus provides a bypass to the conventional cytochrome electron-transfer pathway and allows plants to respire in the presence of compounds such as cyanides and carbon monoxide. There are a number of studies on this problem (e.g., see Affourtit et al. 2000, references therein).

Besides the enzyme, the superoxide ion can also be an electron donor. The ion arises as a result of detoxication of xenobiotics (xenobiotics are outsiders, which are involved in the chain of metabolism). Xenobiotics yield anion-radicals by the neutralizing influence of redox proteins. Oxygen (inhaled with air) takes an unpaired electron off from a part of these anion radicals and forms the superoxide ion. The superoxide ion plays its own active role in biochemical reactions.

2.6 ISOTOPE-CONTAINING ORGANIC COMPOUNDS AS ION-RADICAL PRECURSORS

Isotope substitution aims to ascertain whether a bond labeled with an isotope takes part in a given reaction. One then either looks at the products, noting the label distribution, or attempts to determine the kinetic isotope effect. The latter can be detected as the change in the rate constant of the reaction by using an isotope in the place of an atom taking part in the reaction of interest.

When applied to electron-transfer reactions, this kinetic isotope effect technique can provide information on the real reaction pathway leading to the formation of the product. Frequently, spectroscopic detection of species or identification of products is indicative of radical intermediates. The formation of the intermediates could simply be a blind step.

Isotope-containing organic compounds have important significance as ion-radical precursors in ion-radical organic chemistry. The link between isotopic substitution at the reaction center and change in the kinetic properties is not so obvious in one-electron transfer. In this case, the HOMO of a donor loses one electron. This electron is then shuttled to the lowest unfilled molecular orbital of an acceptor. Therefore, one should expect to see the isotopic effect in electron-transfer reactions as being dependent on the change in the corresponding orbital energy levels of the donor and acceptor as a result of isotopic substitution. Theory shows that electron transfer causes the perturbation in the vibronic levels of a molecule (Efrima and Bixon 1974). For the reactions in solutions (the most typical conditions in synthetic organic chemistry), there is an observed disturbance in the vibronic levels of a complex system, consisting of a donor and an acceptor (the reactants), as well as the solvent itself. The transfer of an electron is defined with a difference between the electron affinity of the acceptor (E_A) and ionization potential of the donor (I_D). The solvent effect on this process is mainly dependent on its reorganization energy accompanying transformations of reactants into products (ΔE_S). It should be noted that the transfer of an electron brings about a sudden change in substrate polarity and results in a cardinal change of a solvate shell. Hence, isotopic substitution can have an effect on electron-transfer reaction only if the following two conditions are satisfied: (1) E_A

or I_D changes and (2) this change is greater than that of ΔE_S. In other words, $\Delta I_D > \Delta E_S$ or $\Delta E_A > \Delta E_S$ (Johnansen and Schoen 1980).

Concerning the change in E_A or I_D for isotopic substitution, currently there is not much data and the exact pattern of the phenomenon is still not known. Nevertheless, it seems useful to compare the existing data both for the consideration of isotopic effects in reactions and for information on the possible new ways of using electron transfer for a more effective enrichment of isotopic mixtures with one specific isotope form.

2.6.1 Kinetic Isotope Effects in Electron-Transfer Reactions

Deuterium substitution reduces the electron affinity of organic substrates. The reduced electron affinity of deuterium-substituted analogs is due to the larger electron-donating effect of deuterium when compared to hydrogen. Its inductive constant is small but negative (−0.0011). The deuterium electron donor effect develops in organic ion-radicals also.

The formation of *N,N′*-dialkyl-4,4′-bipyridine cation-radical proceeds through the reduction of the corresponding dication (alkylviologen) by tributylphosphine. Yasui et al. (2001) measured the reaction kinetics in the acetonitrile–methanol mixture. The rate of cation-radical formation decreases in all of the cases when the alkyl groups are deuterated.

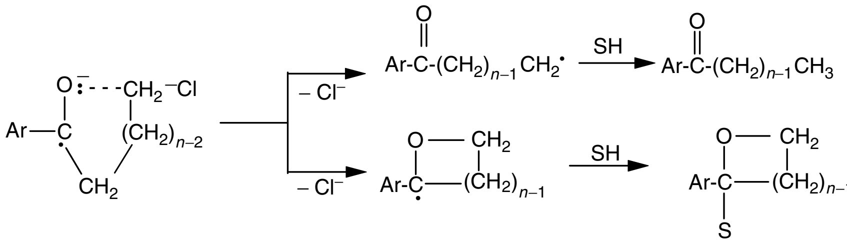
Dimethylsulfide accelerates the decomposition of *tert*-butylperoxybenzoate (Pryor and Hendrickson 1983). Dimethylsulfide acts as a donor, whereas the peroxide acts as an acceptor. Strictly under the same conditions, the rate of the peroxide dissociation in the presence of Me_2S is almost 1.5 times greater than that in the presence of $(CD_3)_2S$ (Pryor and Hendrickson 1983).

The oxidation reaction of alkylaromatic compounds with cerium-ammonium nitrate in acetic acid medium is crucial for the exposition of the problem (Baciocchi et al. 1980): ArMe + Ce(IV) = $ArMe^{+\bullet}$ + Ce(III). Hexamethylbenzene and 4-methoxytoluene are oxidized easily. However, the reaction is slowed down considerably on addition of Ce(III) and the equilibrium is shifted left (toward the reagents), as expected. The abrupt increase in the $^{H}k/^{D}k$ ratio is, nevertheless, not expected and is due to concomitant deprotonation of $ArMe^{+\bullet}$ by the following mechanism: $ArCH_3^{+\bullet} + AcO^- \rightarrow ArCH_2^{\bullet} + AcOH$. This reaction is not significant when the electron-transfer equilibrium is shifted toward the right. Because acetic acid is weakly dissociated, the binding of acetate by an "alien" proton from $ArMe^{+\bullet}$ leaves the "own" proton free to suppress the acid dissociation further. This results in a deficit of acetate ions. However, when the electron-transfer equilibrium is shifted to the left, there is a decrease in the amount of $ArMe^{+\bullet}$ radicals. Therefore, a relative excess of the acetate ions is formed. It makes deprotonation of the radical a rate-limiting step. That the ^1H being transferred is substituted for ^2H is the reason for the growth of $^{H}k/^{D}k$ ratio, that is, an increase in the kinetic isotopic effect. Such a mechanism of "switch from one rate-limiting step to another" is also used in oxidations of alkylbenzenes with tris(phenanthrolene)iron (III) (Schlesener et al. 1984, Schlesener and Kochi 1984) and with manganese triacetate in acetic acid (Andrulis et al. 1966, Eberson 1967). If the rate-determining step is the electron transfer, then the kinetic isotope effect is not very significant.

As assumed, the small and positive value of H/D kinetic isotope effect may be used as a criterion for an electron-transfer pathway. For example, anion-radicals of α-benzoyl-ω-haloalkanes can react in two routes (Kimura and Takamuku 1994). The first route is the common one—an electron is transferred from the oxygen anion of the carbonyl group to a terminal halogen. The transfer provokes fission of the carbon–halogen bond. The second route is the S_N2 reaction, leading to a cyclic product as shown in Scheme 2.37.

In Scheme 2.37, SH is a solvent (hexamethylphosphotriamide). For halogen–hydrogen substitution in $^{-}OCH^{\bullet}-(CH_2)_{n-1}CH_2Cl$ and $^{-}OCH^{\bullet}-(CH_2)_{n-1}CD_2Cl$, the magnitudes of $^{H}k/^{D}k$ are calculated as 1.059 at $n = 2$ and 1.141 at $n = 3$, respectively. The calculated magnitudes of $^{H}k/^{D}k$ for the cyclization route are 0.996 ($n = 2$) and 0.992 ($n = 3$), respectively (Sastry et al. 1995).

Interestingly, the anion-radical from $RC_6H_4CO(CH_2)_4CH_2Br$ reacts according to the halogen–hydrogen substitution, whereas the anion-radical from $RC_6H_4CO(CH_2)_3CH_2Br$ takes the cyclization



SCHEME 2.37

route (Kimura and Takamuku 1994). The choice of the route is dependent on the spatial structure of the transition state. This means dependence on a distance between $^{-}$O and CH_2–Hal fragments and an orientation of the orbitals of a radical pair formed by the concerted electron-transfer and bond-breaking processes.

For the reactions of MeLi with benzophenone and the benzophenone that was labeled at the carbon atom of the carbonyl group, $^{12}k/^{14}k$ ratio is 1.000 in ether at 0°C. Under the same conditions, this ratio is 1.023 for MeLi addition to the carbonyl $^{12}C/^{14}C$ pair of 2,4,6-trimethylbenzophenones (Yamataka et al. 1987a). The very different isotope effects on addition of MeLi to benzophenone and 2,4,6-trimethylbenzophenone were attributed to the difference in the rates of reactant–substrate mixing and reacting, in the same chemically rate-determining step (Maclin and Richey 2002). Mixing is slower than addition to benzophenone, masking inherent differences between the isotopomers and mixing is faster than addition to a very sterically hindered 2,4,6-trimethylbenzophenone. The $^{12}k/^{14}k$ value of 1.023 can be admitted as an intrinsic one.

In the same reaction environment, this ratio is 1.029 for Me_2CuLi and 1.050 for MeMgBr (Hiroshi et al. 1987, Yamataka et al. 1987b, 1989, Matsuyama et al. 1988). For MeMgBr in ether at 20°C, $^{12}k/^{13}k$ ratio was found to be 1.030 (Holm 1993). The magnitudes of $^{12}k/^{14}k$ and $^{12}k/^{13}k$ are in accord "since the origin of kinetic isotope effects lies exclusively in the difference in molecular mass and ^{13}C effect should be on the order of one-half of the ^{14}C effect" (Holm 1993). Hence, in the case of MeLi, one-electron transfer is a rate-limiting step; and for Me_2CuLi and MeMgBr, a rate-determining step is the ion-radical pair recombination by the following mechanism:

$$Ph_2C{=}O + MeMgBr \rightarrow [Ph_2C^{\bullet}{-}O^{-} \cdot (MeMgBr)^{+\bullet}] \rightarrow Ph_2C(Me)OMgBr$$

One should be aware, however, that none of the Grignard reactions of benzophenone proceeds through a completely free coupling process of benzophenone anion-radicals with alkyl radicals. For example, the portion of electron-transfer pathway in the Grignard reactions of benzophenone with isomeric C_4H_9MgCl was estimated to be 65, 61, and 26% for $(CH_3)_3C$–, $CH_3CH_2CH(CH_3)$–, and $CH_3CH_2CH_2CH_2$–, respectively (Lund et al. 1999).

According to the kinetic isotope effect test, the reaction of benzaldehyde with lithium pinacolone enolate proceeds through the polar addition mechanism (Yamataka et al. 1997). As it turned out, the mechanistic switching relates to the stability of the reactants measured by the intrinsic acidity of the conjugate acids RH of R^{-} anions in the gas phase. The reactant whose conjugate acid is most acidic reacts with benzaldehyde through the polar addition mechanism, whereas the reactants whose conjugate acids are less acidic go through the electron-transfer pathway (Yamataka et al. 2001).

As logical as this diagnostic method is, one needs to realize its lack of absolute applicability. The observed magnitude of the kinetic isotopic effect is not great, and the aforementioned statement of independence of the electron affinity from the increase in molecular mass of the substrate is not obvious. This postulate should be proved in each case. Benzophenone, taken as an isotopic mixture of $^{12}C{=}O$ and $^{13}C{=}O$ gives a mixture of anion-radicals with a decreased proportion of $^{13}C{=}O$ isotomer when reduced with potassium in HMPA (Stevenson et al. 1987b). In effect, this means that for the heavier isotopomer of benzophenone, the electron affinity is smaller.

Until now, the isotopic effect was discussed only in relation to the reactants. In electron-transfer reactions, the solvent plays an equally important role. As mentioned, different solvate forms are possible for reactants, transition states, and products. Therefore, it seems important to find a reaction where the kinetic effect resulting from the introduction of an isotope would be present for solvents, but absent for reactants. For a published work concerning this problem, refer Yusupov and Hairutdinov (1987). In this work, the authors studied photoinduced electron transfer from magnesium ethioporphyrin to chloroform followed by a dark recombination of ion-radicals in frozen alcohol solutions. It was determined that the deuteration of chloroform does not affect the rate of transfer, whereas deuteration of the solvent reduces it. The authors correlate these results with the participation of solvent vibrational modes in the manner of energy diffraction during electron transfer.

Electron-transfer reactions deal with ionic participants. It might, therefore, be worthwhile to bear in mind that replacing the solvent with its deuteriated analogue may also result in some perturbations in the delicate interactions between the anion-radical and counterion. As shown, substitution of hydrogens with deuteriums results in a slight increase in the polarity of THF (Stevenson et al. 1991a). The effect is understandable due to the electron-donating nature of deuterium relative to hydrogen. The increased solvent polarity augments solvent ability to charge separation. The charge separation may change the anion-radical reactivity, of course.

2.6.2 Behavior of Isotope Mixtures in Electron-Transfer Reactions

It is clear that deuterium as a substituent has the electron-donating effect. In other words, it can decrease electron affinity of the whole molecule. Potentials of reversible one-electron reduction for naphthalene, anthracene, pyrene, perylene, and their perdeuteriated counterparts indicate that the counterparts exhibit slightly more negative potentials (Goodnow and Kaifer 1990, Morris and Smith 1991). For example, the measurable differences in the reduction potentials are equal to −13 mV for the pair of naphthalene–naphthalene-d_8 or −12 mV for the pair of anthracene–anthracene-d_{10}. The possible experimental error does not exceed 2 mV (Morris and Smith 1991). In another example, in DMF with 0.1 M n-Bu_4NPF_6, the deuterated pyrenes were invariably found to be more difficult to reduce than pyrene itself. The largest difference observed, −12.4 mV, was between perdeuteriated pyrene and pyrene bearing no deuterium at all with standard deviations between 0.2 and 0.4 mV (Hammerich et al. 1996).

A comparative analysis of vibrational modes of perdeuterobenzene, benzene, and their anion-radicals shows that the deuteration leads to an increase in the level of zero-point energy. Other energy levels of the perdeuterio derivatives are also shifted, and the electron affinity is reduced by almost 2 kJ (Stevenson and Alegria 1976, Stevenson et al. 1986a, Stevenson et al. 1986b). Similarly, the electron affinity is reduced by 1 kJ on changing from $^{12}C_6H_6$ to $^{13}C_6H_6$. A comparable change in the electron affinity should be expected for other classes of organic compounds as well. To verify these estimations experimentally, the analysis of ESR spectra resulting from an incomplete reduction of the precisely measured amounts of benzene isotopomers with potassium in THF was conducted (Stevenson et al. 1986a). This approach had been outlined by Chang and Coombe (1971). The superimposed spectra were analyzed to find the intensity ratio of signals belonging to isotopomeric anion-radicals. The ratio produced the relative concentrations of the anion-radicals under consideration.

For example, a 4.5:1 mixture of $^{13}C_6H_6$ + $^{12}C_6H_6$ forms the 2:1 mixture of $(^{13}C_6H_6)^{-\bullet}$ + $(^{12}C_6H_6)^{-\bullet}$ on reduction at −100°C by the half-stoichiometric amount of potassium in THF. Therefore, the heavier anion-radical amount is less than the amount of the heavier parental substrate in the initial mixture. The ESR data were reproduced by means of nuclear magnetic resonance (NMR) and mass-spectral methods after transformation of anion-radical mixtures into mixtures of corresponding neutral compounds and removal of the solvent.

For the equation $(C_6H_6)^{-\bullet}K^+ + C_6D_6 = C_6H_6 + (C_6D_6)^- K^+$, the ratio of isotopomers before and after the electron transfer can be recalculated into the corresponding equilibrium constants. Table 2.1 gives the order of these constants and experimental conditions typical for their determination.

TABLE 2.1
Equilibrium Constants (K_{eq}) of Electron-Transfer Reactions

Entries	Starting Aromatic Compound	Starting Anion-Radical Salt	°C	Solvent	K_{eq}	Reference
1	C_6D_6	$(C_6H_6)^{-\bullet}K^+$	−100	THF	0.27	SER'86
			+25	THF	0.46	SWR'91
2	t-BuC_6D_5	$(t\text{-}BuC_6H_5)^{-\bullet}K^+$	+25	THF	0.36	SWR'91
3	$MeOC_6D_5$	$(MeOC_6H_5)^{-\bullet}K^+$	+25	THF	0.39	SWR'91
4	$C_6H_5{-}C_6D_5$	$(C_6H_5{-}C_6H_5)^{-\bullet}K^+$	+25	HMPA	0.51	SWR'91
5	$N{\equiv}CC_6D_5$	$(N{\equiv}CC_6H_5)^{-\bullet}K^+$	+25	HMPA	0.70	SWR'91
6	$O_2NC_6D_5$	$(O_2N\,C_6H_5)^{-\bullet}K^+$	+25	NH_3(liq)	0.86	SWR'91
7	Naphthalene-d_8	$(Naphthalene)^{-\bullet}K^+$	−100	THF	0.26	SS'90
8	Anthracene-d_{10}	$(Anthracene)^{-\bullet}K^+$	−100	THF	0.30	SS'90
9	Pyrene-d_{10}	$(Pyrene)^{-\bullet}K^+$	−100	THF	0.37	SS'90
10	Perylene-d_{10}	$(Perylene)^{-\bullet}K^+$	−100	THF	0.40	SS'90
11	$(C_6D_5)_2C{=}O$	$[(C_6H_5)_2C{=}O]^{-\bullet}K^+$	−75	NH_3(liq)	0.52	LPR'88 SHK'93
12	$(C_6H_5)_2{}^{13}C{=}O$	$[(C_6H_5)_2C{=}O]^{-\bullet}K^+$	+25	HMPA	0.58	SER'86
13	Benzoquinone ($^{13}C{=}O$)	$(O{=}C_6H_4{=}O)^{-\bullet}Na^+$	−75	THF + CE HMPA	0.66	SHR'93
14	Benzoquinone ($O{=}C_6D_4{=}O$)	$(O{=}C_6H_4{=}O)^{-\bullet}Na^+$	−75	THF + CE HMPA	1.00	SHR'93

Note: SER'86 = Stevenson et al. 1986a; SWR'91 = Stevenson et al. 1991b; SS'90 = Stevenson and Sturgeon 1990; LPR'88 = Lauricella et al. 1988; SHK'93 Stevenson et al. 1993a; SHR'93 = Stevenson et al. 1993b. CE stands for 18-crown-6 ether.

The equilibrium constant for electron transfer from anion-radical salts of aromatic compounds (with the usual isotope content) to neutral molecules of the same compounds containing heavier isotopes is less than unity (entries 1–10 in Table 2.1). This means that for heavier compounds (enriched with neutrons), the electron affinity is smaller. As an addition to the data of Table 2.1, it is interesting to mention the result of reduction of C_6H_6 and $C_6H_5D_1$ mixture. It proceeds in favor of the formation of $C_6H_6^{-\bullet}$ over that of $C_6H_5D_1^{-\bullet}$, and $K_{eq} = 0.86$. This corresponds to a 210 J mol^{-1} smaller electron affinity for monodeuterated benzene than for benzene itself (Stevenson 2007). According to Table 2.1, entry 1, the solution electron affinity was found to decrease further with more added deuterium and, for hexadeuterated benzene, $K_{eq} = 0.27$, that is, by three times lower. The difference in electron affinity between deuterated and nondeuterated analogs is conserved at different temperatures and reaction mediums (including those favorable to the destruction of ionic pairs—in HMPA and THF containing 18-crown-6).

With respect to the ionic pairs, perdeuteration in organic anion-radicals alters the zero-point energies of the vibrational modes involving the interaction of a metal cation with an organic counterpart. As shown, the anion-radical of perdeuteronaphthalene associates with sodium cation in THF more tightly than the anion-radical of perprotionaphthalene under the same conditions (Stevenson et al. 1993c).

The solution electron affinities of a series of monosubstituted benzenes were measured by the ESR method (Stevenson et al. 1991b). The equilibrium constant for the electron transfer in $XC_6H_5^{-\bullet} + XC_6D_5 = XC_6H_5 + XC_6D_5^{-\bullet}$, where X = H, *tert*-Bu, OMe, Ph, CN, was found to be less than unity for all cases (entries 1–6 in Table 2.1). These equilibrium constants are in linear correlation to the appropriate constants σ of the substituents.

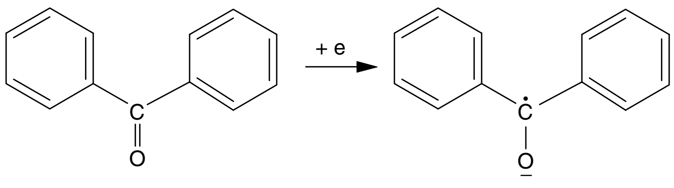
The deuterium isotope effect on homogeneous electron-transfer reactions has been noted for cation-radicals, too. Gronheid et al. (2003) observed the effect for cation-radicals of biphenyl and

its symmetric dimethyl derivatives. As to the nitrogen isotope effect, Lue et al. (2001) reported that the ^{15}N-labeling of *N,N,N′N′*-tetramethyl-*p*-phenylenediamine appreciably decreases the ionization potential of the molecule, making it easier to lose an electron and form the corresponding cation-radical in the AN solution.

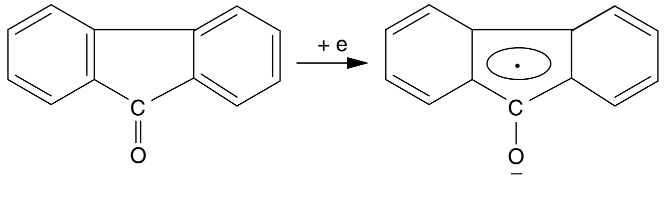
Although the problem of isotope effects in ion-radical organic chemistry is still new and not many examples have been studied, some electron-transfer reactions between an anion-radical and a heavy molecule were found in which the equilibrium constant is greater than one. One can see this in entry 11 of Table 2.1 and from Schemes 2.38 and 2.39. The behavior of benzophenone was a part of the general trend. Fluorenone (Stevenson et al. 1986a) gives the anion-radical mixture in which there is more of $^{13}C^{\bullet}$–O^- (heavier) isotopomer than it contains in the ^{12}C=O and ^{13}C=O mixture before reduction with a small amount of metallic sodium in HMPA. The equilibrium constant of this reaction at 25°C is 2.74 versus the analogous equilibrium constant of 0.58 for the benzophenone reaction under the same conditions. The more recent publications on the subject, by Holm (1994) and Yamataka et al. (1995), give the impression that the problem with benzophenone is still unsettled. Their measurements were performed following Stevenson's preparative procedure (entry 11 in Table 2.1) except for the use of higher ketone/ketyl concentrations and sodium instead of potassium. The solvent, NH_3(liq), was the same. The use of gas chromatography (GC) (Holm 1994) or Fourier transform ion cyclotron resonance (FTICR) technique (Yamataka et al. 1995) instead of quantitative ESR and mass spectroscopy has changed the analytical part of the procedure. Holm and Yamataka et al. have obtained the values of the equlibrium constants that are different from those obtained by ESR. *Ab initio* calculations at the high level were consistent only with the newly obtained values (upto 1.05–Yamataka et al. 1995). Of course, the experimental vagaries might cause such discrepancies in the evaluation of the equilibrium isotope effect. At this time, it is difficult to choose one result over another. However, a further comparison between benzophenone and fluorenone is done by using Stevenson's data because they give a logically conjoint pattern. It is relevant to note that an equilibrium constant of less than unity was obtained for the structurally similar pair of phenyl-d_5 cyclopropyl ketone and anion-radical of phenyl-h_5 cyclopropyl ketone (Tanko and Drumright 1992).

In the case of the anion-radical of benzophenone, the effect of an added electron is not very specific: It results in weakening of multiple bonds and strengthening of single bonds. Such an effect is usual for all organic anion-radicals. One-electron reduction of benzophenone, a fully conjugated ketone, yields a ketyl and results in the general bond loosening (Scheme 2.38).

In case of fluorenone, the situation is reversed. A general bond-order increase is expected when an electron is added to a substituted cyclopentadienone such as fluorenone (Scheme 2.39).



SCHEME 2.38



SCHEME 2.39

Stevenson et al. (1987a) noted that such general bond tightening results in a decrease of the sum of all the frequencies over all vibrational degrees of freedom in fluorenone. The vibrational frequencies are inversely proportional to the square root of the reduced masses of the atoms involved. It means that the difference between the mentioned sums is greater for ^{13}C-substituted systems than for ^{12}C systems. Since bonds are tightened on one-electron addition, they are tightened more for ^{13}C-substituted material. From this, the authors predicted that "the zero-point energy effects would result in fluorenone having a lower electron affinity than fluorenone substituted at the carbonyl position with a ^{13}C." The experiment confirmed these predictions.

For the *p*-benzoquinone series (Table 2.1, entries 13 and 14), the equilibrium isotope effect (confirmed through physical separation of the isotopic isomers involved) was observed by means of ESR analysis (Stevenson et al. 1993a, Stevenson et al. 1993b). In this case (entry 13), the equilibrium constant is equal to 0.66. An analogous competition for an electron between *p*-benzoquinone and perdeuterated *p*-benzoquinone (entry 14) shows no equilibrium isotope effect. For benzoquinone ($^{13}C{=}O$), the ^{13}C effect is attributed almost exclusively to the carbonyl group. The constant of electron exchange equilibrium between benzoquinone $O{=}^{13}C_6H_4{=}O$ and $(O{=}C_6H_4{=}O)^{-\bullet}Na^+$ is 0.63 in THF + HMPA at –75°C. The low spin density on the noncarbonyl positions renders the substitution of the protons by deuteriums and the noncarbonyl carbons by ^{13}C ineffective by altering the electron affinity in the solution. The most significant decrease in vibrational frequency on electron addition was indeed observed in the C=O stretch (Chipman and Prebenda 1986).

Nevertheless, rigorous and detailed calculations (Jacob et al. 1999) did not support the large heavy-atom isotope effect determined from ESR experiments on electron transfer with the participation of benzoquinone. Equilibrium constants involving ^{13}C-, ^{17}O-, and ^{18}O-labeled species were predicted not to deviate significantly from unity. At the same time, a large isotope effect is expected for the process with deuterium substitution, reflecting the importance of the large change in reduced masses (deuterium mass is double with respect to protium mass). The discrepancy between theory and experiment cannot be attributed to the role of the counterion. A redetermination of the equilibrium isotope effects using alternative experimental techniques would be of interest. The case with *p*-benzoquinone is very important in terms of the regioselectivity of the effect discussed.

In the case of cyclooctatetraene, an electron "prefers" the isotopically heavier material. At 173 K, the equilibrium constant for $C_8H_8^{-\bullet} + C_8D_8 = C_8H_8 + C_8D_8^-$ was found to be 1.16 (Stevenson 2007). However, when this anion-radical reacts with cyclooctatetraene dianion (not with the anion-radical), the transferred electrons *prefer* the isotopically lighter material (Stevenson et al. 1990, 1992) as follows: $C_8H_8^{-\bullet} + C_8D_8^{2-} = C_8H_8^{2-} + C_8D_8^{-\bullet}$. The semiempirical quantum chemical consideration led to the conclusion that the discrepancy can be a consequence of the ion-pair formation (Zuilhof and Lodder 1995). In the case of cyclooctatetraene, the ion-pairing phenomenon deserves a more detailed explanation. Although the dianion of cyclooctatetraene is completely planar and meets all the requirements of aro maticity, the anion-radical of cyclooctatetraene is a nonaromatic species and is not completely planar. In the equilibria just considered, both the anion-radical and the dianion had alkali cations as counterparts. The dialkali salt of the dianion has two cations symmetrically located over and beneath the octagonal plane. Distortions from ion pairing between the dianion plane and these two alkali cations are reciprocally compensated. With the slightly puckered anion-radical of cyclooctatetraene, the rigid ion pairing is possible. Analysis of vibrational fine structure in the absorption and emission spectra of the potassium salt of cyclooctatetraene anion-radical in a matrix has shown the formation of a rigid ion pair (Dvorak and Michl 1976). The rigid ion pairing restricts ring breathing and out-of-plane bending vibrations, which contribute significantly to the overall isotope effect (Zuilhof and Lodder 1992).

The solution electron affinity of C_8D_8 proved to be slightly greater than that for C_8H_8. Cyclooctatetraene is [8]annulene. For [16]annulene, the solution electron affinity of $C_{16}D_{16}$ is normally lower than that of $C_{16}H_{16}$. NMR experiments reveal that the barrier to ring flattening is greater in the $C_{16}D_{16}$ system than the $C_{16}H_{16}$ system. Coupled with the prediction of density functional theory that $C_{16}D_{16}^{-\bullet}$ is nearly planar, the data account for the normal equilibrium isotope effect is observed in the electron transfer (Kurth et al. 1999, Stevenson and Kurth 1999).

An interesting but still unexplained case refers to nitrobenzene. The reversible electron exchange between nitrobenzene-^{15}N and sodium salt of the nitrobenzene-^{14}N anion-radical is characterized by the usual constant of 0.40. Stevenson et al. (1987b) used NH_3(liq) as a solvent for these measurements at −75°C. Under the same conditions, they obtained the equilibrium constant of 2.1(!) for the electron exchange between nitrobenzene-^{15}N and the potassium salt of nitrobenzene-^{14}N anion-radical. Perhaps, the difference between ion radii of sodium and potassium cations is crucial for the stability of the corresponding ion pair with nitrobenzene anion-radical. Such diversity can be pivotal when the electron prefers the *heavy* or *light* nitrobenzene.

The future will supposedly bring a more precise description of the trends considered here, and the reasons for the exceptions will be clearer. It is quite possible that in this field, too, the exceptions will only confirm the rule. For now, it is worth concluding that all these regularities have very real practical applications. It is a fact that the equilibrium constants of the previously described reactions differ from unity. This provides an opportunity to separate and enrich isotopic mixtures.

For instance, the effect of deuterium substitution on the electron exchange has been studied for the thianthrene cation-radical and its neutral molecular precursor (Liu et al. 1992). The corresponding equilibrium constant was determined to be 0.62. The authors underlined that such an isotope effect may be used for isotopic enrichment. Before that, Stevenson et al. (1986c) proposed a separation method for the natural mixture of nitrobenzenes containing ^{14}N and ^{15}N isotopomers. A solution of 0.03 and 0.08 mmol of $Ph^{15}NO_2$ and $PhNO_2$, respectively, were treated with 0.01 mmol of potassium metal in dehydrated liquid NH_3. After the evaporation of NH_3, the mixture of the initial compounds with their anion-radical potassium salts remains to be further treated. The neutral nitrobenzenes are liquids; they are distilled out under high vacuum. The rest is solid. The solid remainder is oxidized with a solution of iodine in ether: $PhNO_2^{-\bullet}K^+ + ½\,(I_2) \rightarrow KI + PhNO_2$. The resulting mixture contains twice as much $Ph^{15}NO_2$ as the starting mixture (the equilibrium constant of electron transfer is approximately 2). On repetition of the procedure, the $Ph^{15}NO_2$ content in the mixture is increased twofold, and so on. The natural nitrobenzene sample with $Ph^{15}NO_2$ content of 0.37% only was enriched up to the nitrobenzene-^{15}N of 99% purity after 16 repetitions of the treatment described earlier. This kind of physical separation of neutral molecules and anion-radicals is, of course, a very unusual and effective way to enrich isotopic mixtures.

In case of benzene, the potassium salt of its anion-radical can be separated as a precipitate after benzene reduction by potassium in the presence of low concentrations of 18-crown-6-ether. For benzene, the heavy-form content is greatest in the solution, not in the precipitate. It is in the solution where most of the nonreduced neutral molecules remain. Since the neutral molecules are inert toward protons, the anion-radicals combine with the protons to give dihydro derivatives (products of the Birch reaction). Therefore, it is possible to conduct the separation chemically. The easiest way is to protonate a mixture after the electron transfer, than to separate the aromatic compounds from the respective dihydroaromatics (cyclohexadiene, dihydronaphthalene, etc.) (Chang and Coombe 1971, Stevenson and Alegria 1976; Stevenson et al. 1986a, 1986c, 1988).

This chemical way to enrich the isotope-containing mixtures is easier and more effective than many other methods that are currently in use. The formation of dihydro derivatives in the Birch reaction can, obviously, occur not only by protonation of an anion-radical but also of dianion. For example, the anion-radical $C_{10}H_8^{-\bullet}$ can easily acquire another electron to give the dianion $C_{10}H_8^{2-}$. Then, a two-step protonation gives dihydronaphthalene: $C_{10}H_8^{2-} + H^+ \rightarrow C_{10}H_9^- + H^+ \rightarrow C_{10}H_{10}$. This is why an important question should be raised: Can the direction of isotopic enrichment, outlined for anion-radicals, be extended to apply to dianions as well? Experiments concerning the reduction of a mixture of anthracenes $C_{14}H_{10} + C_{14}D_{10}$ and perylenes $C_{20}H_{12} + C_{20}D_{12}$ with excess amounts of potassium in THF give an answer to this question (Stevenson et al. 1986a). The reduction of these 1:1 mixtures results predominantly in nondeuterated anion-radicals. However, on subsequent reduction (with the transfer of the second electron), the relative concentration of deuteriated anion-radicals increases, and these particles are the main paramagnetic products after dissolution of 2 mol

of potassium per 1 mol of hydrocarbon. The reactions with the corresponding constants determined at −100°C are listed as follows:

$$C_{14}H_{10}^{2-}2K^{+} + C_{14}D_{10}^{-\bullet}K^{+} = C_{14}H_{10}^{-\bullet}K^{+} + C_{14}D_{10}^{2-}2K^{+} \quad {}^{H}k/{}^{D}k = 0.74$$

$$C_{20}H_{12}^{2-}2K^{+} + C_{20}H_{12}^{-\bullet}K^{+} = C_{20}H_{12}^{-\bullet}K^{+} + C_{20}D_{12}^{2-}2K^{+} \quad {}^{H}k/{}^{D}k = 0.65$$

By comparing these constants with the equilibrium constants of anion-radical reactions (entries 7–10 in Table 2.1), one can conclude that in case of dianions, the equilibrium is definitely shifted to the right. The equilibrium constants of ca. 0.35 are increased almost twofold, up to approximately 0.7, but remain less than unity. This means that even with the formation of dianions, the possibility of isotopic enrichment still remains quite feasible, although the process becomes less favorable than that in the case of nitrobenzene.

The difference in the electron affinity between light and heavy isotopic isomers is, in other words, the difference in the stability of their anion-radicals. Such a difference gives a valuable tool for use in probing the chemistry of anion-radicals. The difference in the stability of the ring-deuterated and ring-nondeuterated arene anion-radicals has been employed to examine the transition states for the one-electron-promoted cleavage of naphthyl methyl phenyl ether and naphthyl benzyl ether (Guthrie and Shi 1990). In this reaction, the potassium salt of fluoranthene anion-radical was an electron donor:

$$C_6H_5OCH_2C_{10}H_7 + e \rightarrow C_6H_5OCH_2C_{10}H_7^{-\bullet} \rightarrow C_6H_5O^{-} + {}^{\bullet}H_2CC_{10}H_7$$

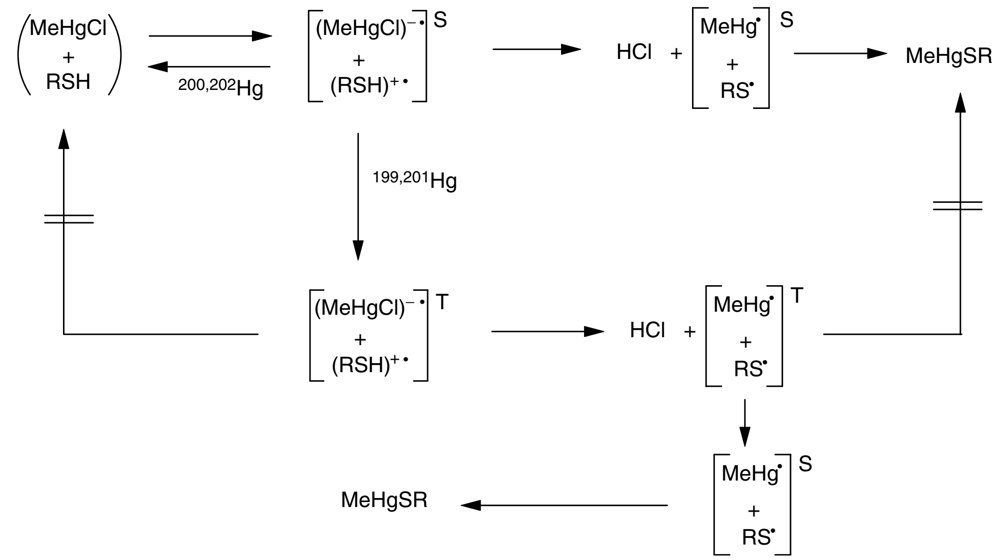
$$C_6H_5CH_2OC_{10}H_7 + e \rightarrow C_6H_5CH_2OC_{10}H_7^{-\bullet} \rightarrow C_6H_5CH_2^{\bullet} + {}^{-}C_{10}H_7$$

The starting material $C_6H_5OCH_2C_{10}H_7$ reacted more easily than $C_6H_5OCH_2C_{10}D_7$. Equimolar mixtures of D- and H-naphthyl methyl phenyl ethers were reduced by the one-electron donor. The product mixture of this cleavage was found to contain an excess of nondeuterated methylnaphthalene. Conversely, the remaining unchanged material contains an excess of the naphthalene-ring-deuterated ether. Obviously, in the rate-determining step (i.e., scission of the $CH_2{-}O$ bond), the corresponding transition state resembles a naphthalene anion-radical. In the transition state, the added electron remains localized in a π* molecular orbital. Clearly, to the extent that naphthalene-ring-deuteration raises the energy of the transition state relative to that of its unsubstituted isotopic isomer, fractionation must occur on proceeding from the ether (reactant) to methylnaphthalene (product).

Meanwhile, the described methods of fractionation came into general synthetic practice. For instance, mesitaldehyde-3,5-d_2 was prepared by reaction of mesitaldehyde with D_2SO_4 following up to the arene protio-deuterio exchange method (Jiao et al. 2007).

Rathore et al. (2006) studied the intramolecular single-electron transfer in anion-radicals formed from fluorenylidene derivatives. The derivatives used for the reduction were Me—Flu—CH_2—Flu—CH_2—Flu—CH_2—Flu—Me and its deuterated analog, Me—Flu—CH_2—(Flu-d_8)—CH_2—(Flu-d_8)—CH_2—Flu—Me. Each parent compound initially gave an anion-radical in which an unpaired electron was tunneled between the two internal Flu nuclei and then occured within the outer Flu nuclei. In the outer part, coordinative solvation of the anion-radical by HMPA proceeded much more effectively because of ready space accessibility. Such a solvation provides a driving force for electron tunneling. As the solution electron affinities of perdeuterated aromatic hydrocarbons are less than those of perprotiated hydrocarbons, the electron tunneling was found to be at least an order of magnitude faster only in the case of [Me—Flu—CH_2—(Flu-d_8)—CH_2—(Flu-d_8)—CH_2—Flu—Me]$^{-\bullet}$.

Isotope effects on redox reactions of the type considered in Section 2.6 are of interest for a number of reasons. At a fundamental level, the magnitude of the effect provides an important clue to the electronic structure and vibrational properties of the species involved. From a practical point of view, a large deviation from unity for the equilibrium constant offers a convenient procedure for the enrichment of the isotopomer mixtures.



SCHEME 2.40

Completing the consideration of isotopic effects in the electron-transfer reaction, the reaction of creatine kinase (denoted as RSH) with methylmercury chloride, CH_3HgCl, is mentioned. Buchachenko et al. (2004) observed some inhibition of enzymatic activity of RSH by CH_3HgCl. The effect is appreciable for magnetic (^{199}Hg, ^{201}Hg) isotopomers and is absent for nonmagnetic (^{200}Hg, ^{202}Hg) isotopomers. When the mercury isotopes in CH_3HgCl are present in natural abundance, the reaction with RSH fractionates the magnetic and nonmagnetic isotopomers. Scheme 2.40 was proposed to illustrate this finding.

Scheme 2.40 is explained as follows. The ^{200}Hg and ^{202}Hg isotopes have neither nuclear spin nor magnetic moment, whereas ^{199}Hg and ^{201}Hg have nuclear spins of 1/2 and 2/3, respectively, as well as magnetic moments of +0.5029 and −0.5602 μ_B, respectively. Magnetic nuclei ^{199}Hg and ^{201}Hg interaction with an unpaired electron of $(MeHgCl)^{-\bullet}$ induces a nonbarrier singlet–triplet conversion (S → T). This conversion is prevented in the case of ^{200}Hg and ^{202}Hg isotopes, and only back electron transfer takes place. In the case of ^{199}Hg and ^{201}Hg, the MeHgCl regeneration at the expense of back electron transfer is spin forbidden, and the only chemically available channel is the release of an HCl-generating triplet pair of neutral radicals [MeHg$^\bullet$ $^\bullet$SR]. This pair undergoes the fast and reversible T → S spin conversion, which stimulates the recombination of the pair. The magnetically different reactions considered here shed new light on the toxic action of methylmercury chloride, which is an environmental and occupational hazard, promoting a severe neurological disorder known as Minamata disease.

2.7 ORGANIC ION-RADICALS IN SOLID PHASES

2.7.1 Organic Ion-Radicals in Frozen Solutions

Many organic compounds form ion-radicals, which are unstable in the liquid phase. In such cases, pulse radiolysis in frozen solutions is used, although the energy of the incoming electron is much larger than that in the liquid-phase reactions of one-electron transfer. Accordingly, the incipient ion-radicals are imparted with excess energy. Sometimes, the sample is included in the rare gas and nitrogen matrices. Knight and Ebner (1976) gave apt description of the technique.

Let us first discuss relations between the nature of the matrix and the fate of the ion-radicals generated. Photoionization in rare gas matrix (when no electron acceptor is added) transforms aromatic

hydrocarbons into cation-radicals but with yields not more than 15%. In cryogenic water ice, the yields exceed 70%. In the gas matrix, back electron transfer is the major phenomenon. Rare gas matrices are formed at the expense of van der Waals forces, whereas ice matrices are formed by much stronger hydrogen bonds. In ice matrices, solvating of both ions and electrons takes place. This prevents back electron transfer to a great extent. The cation-radicals formed are stable at 15 K for a long period of time. Cryogenic ice is transparent and excellent to undertake spectroscopic studies in the region of 250–900 nm. The interval of working temperatures is from 15 to 50 K. The cation-radicals are converted to the corresponding alcohols at temperatures higher than 50 K (Gudipati 2004).

More often, organic solvents are used. Bally et al. (2006) compared the stability of the dicyclopropylidenemethane cation-radical generated by the γ-irradiation of the parent molecule in frozen Freon solution with that by x-ray irradiation in argon matrices. In Freon, the structure of the initial neutral precursor was retained up to 150 K. In argon, the ring-opening product, the cation-radical of (2-methylallylidene) cyclopropane, was formed. This dissimilarity is caused by the difference in ionization energy (IE): 15.75 and 10–11 eV in argon and Freon, respectively. Another effect of the nature of a matrix consists of molecular diffusion that sometimes takes place in the solid systems. This kind of diffusion can lead to the formation of dimeric cation-radicals (see, e.g., Itagaki et al. 2002). To observe just a primary cation-radical, fluorotrichloromethane is recommended as a matrix. This polycrystalline medium allows the recording of well-resolved ESR spectra and does not assist in any diffusion-induced bimolecular reactions.

In experiments where ion-radicals are generated by radiolytic reduction or oxidation in solid matrices, the concentration of solute molecules must be at least 10^{-3} M to ensure efficient scavenging of the initially generated electrons or holes. At the same time, the upper limit of the solute concentration should not exceed 10^{-2}–10^{-1} M. It is necessary that the direct effect of radiation on the solute molecule should be ignored. This is one of the major requirements for successful use of radiolytic methods for generating ion-radicals.

Radiolytic generation of organic ion-radicals in frozen matrices is conjugated with spectroscopic characterization of the species formed. Therefore, solvents for the matrices must be transparent and express solvency. Even if the chosen solute has a low ionization potential or high electron affinity, poor solute solubility often makes the method inapplicable. To circumvent such a restriction, ionic liquids (alkylammonium and alkylimidazolium salts) were recommended (Marcinek et al. 2001). Ionic liquids are good solvents for a wide range of organic substances. Many of these liquids form transparent, good-quality glasses on freezing at 77 K and can be used over a wide range of temperatures. Most notably, the possibility exists for the generation of both cation and anion-radicals in the same experiment. As the properties of ionic liquids can be controlled to a large extent by variation of the cation and anion counterparts, the desired features can be reached by appropriate design and synthesis.

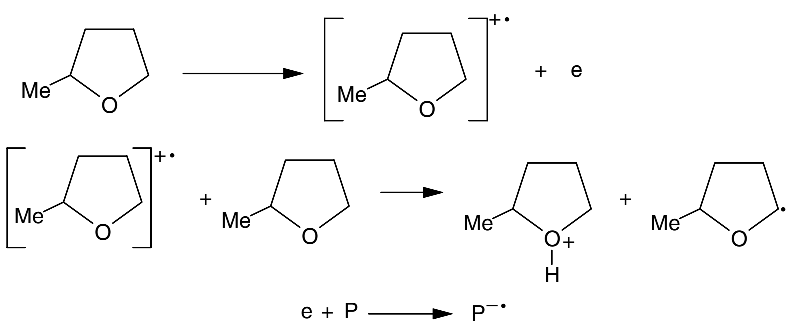
The next topic of our consideration is the ion-radical incipiency. Generally, the mechanism of the ion-radical generation in frozen solution is as follows. Irradiation drives electrons out from a solvent. An organic precursor (P) transforms into an ion-radical. At first glance, two reactions might be expected to take place: electron capture ($P + e \rightarrow P^{-\bullet}$) and electron detachment ($P + e \rightarrow P^{+\bullet} + 2e$). In fact, an indirect redox process takes place, with solvent participation. The example in Scheme 2.41 visualizes 2-methyltetrahydrofuran (MeTHF) participation in the redox process, when P is a substance of electron affinity higher than that of the solvent.

If P is a substance of electron affinity lower than that of the solvent (e.g., AlkHal in SF_6), the process leads to the formation of the cation-radical. If P is a substance of electron affinity higher than that of a solvent (e.g., AlkHal in CH_3OH), the process leads to the formation of the anion-radical. These possibilities are depicted in the following equations, based on alkyl halides:

$$\text{AlkHal} \rightarrow (\text{AlkHal})^{+\bullet} + e$$

$$\text{Alkal} + e \rightarrow (\text{AlkHal})^{-\bullet} \rightarrow \text{Alk}^{\bullet} + \text{Hal}^{-}$$

$$(\text{AlkHal})^{+\bullet}\text{P} \rightarrow \text{AlkHal} + \text{P}^{+\bullet}$$



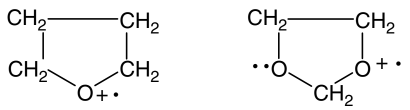
SCHEME 2.41

Addition of a large concentration of toluene or benzene to AlkHal increases the yield of $P^{+\bullet}$, sometimes by a factor of 2.5. The increased yield was found for those Ps whose redox potential is near 1.1 V (against saturated calomel electrode), such as biphenyl, anthracene, pyrene, trialkylamines, oligothiophenes (Funston and Miller 2005). This effect was described for laser pulse radiolysis of the solutes in 1,2-dichloroethane solutions and is supposedly applicable to frozen matrices of alkylhalides in general. The authors guess that the enforcement of $P^{+\bullet}$ formation is caused by the appearance of additional (not very strong) oxidizers in the system. One of these oxidizers is the benzene or toluene complex with chlorine atom, ArH-π-Cl•. The atomic chlorine is an understandable participant of the process: $Cl^- + (AlkCl)^{+\bullet} = AlkCl + Cl^\bullet$. The ArH-π-Cl• complex formed is a long-lived species and can react with a substrate P: $ArH\text{-}\pi\text{-}Cl^\bullet + P \rightarrow (P^{+\bullet}, Cl^-) + ArH = P^{+\bullet} + Cl^- + ArH$. Another new oxidizer is $(ArH)^{+\bullet}$ originating from the following reaction: $ArH + (AlkCl)^{+\bullet} \rightarrow AlkCl + (ArH)^{+\bullet}$. The latter attacks P according to the electron exchange scheme: $P + (ArH)^{+\bullet} \rightarrow ArH + P^{+\bullet}$. As a whole, the process of $P^{+\bullet}$ generation proceeds with an enhanced efficacy.

There are organic precursors that generate both cation- and anion-radical under radiolysis. This is especially important for the emerging field of "plastic solar." Thus, a conjugated polymer, polyfluorene, gets hold of the cation-radical fragments on radiolysis in 1,2-dichloroethane. In THF, the same polymer acts as an electron acceptor, acquiring the anion-radical regions (Takeda et al. 2006).

The generation of ion-radicals usually proceeds in frozen diluted solutions at 77 K and under irradiation for not more than half an hour. An ion-radical concentration of 10^{-4}–10^{-3} is reached, which is sufficient to record optical or ESR spectra of the ion-radicals. The solvents must form transparent matrices as they get cold. For example, THF gives opaque glasses, which prevent any spectral studies, whereas MeTHF ($C_5H_{10}O$) does form ideal glacial matrices at 77 K. However, these samples contain the radical $^\bullet C_5H_9O$ (see Scheme 2.41), and its ESR signal is often superposed over that of the dissolved anion-radical $P^{-\bullet}$. In other glass-making solvents, good spectra with superfine structures are achievable. Tetramethylsilane for anion-radicals and trichlorofluoromethane ($CFCl_3$) for cation-radicals are recommended (Shida et al. 1984). The latter solvent ($CFCl_3$) can be substituted by $CF_2ClCFCl_2$; in $CF_2ClCFCl_2$ glasses, even such unstable species such as 3-methylpentane and 3-methylhexane cation-radicals give an excellent ESR spectra (Ohta and Ichikawa 1987). The aromatic cation-radicals in the $CFCl_3$ matrix have a tendency to form partially oriented samples in which the amount of order/disorder depends on the concentration of the solute and freezing rate. This brings its own obstacles in spectral studies. Meanwhile, the aromatic cation-radicals in CF_3CCl_3 matrix form only glassy samples (Kadam et al. 1999).

A simple method for the production and cryogenic trapping of ion-radicals is mentioned. The technique, cold window radical discharge (CWRD), enables the isolation of short-lived species in rare gas matrices, such as *p*-dichlorobenzene cation-radical. These species are formed within discharge plasmas, close to the trapping surface (Kolos 1995).



SCHEME 2.42

Let us consider several examples of the glass method application. Cation-radicals of substituted benzenes were prepared by γ-radiation of dilute frozen solutions in $CFCl_3$ at 77 K (Ramakrishna Rao and Symons 1985). According to ESR spectra and quantum-mechanical calculations, an unpaired electron is preferentially localized in the framework of the phenyl ring of cation-radicals of benzaldehyde and acetophenone. Styrene and its derivatives give cation-radicals in which an unpaired electron spends 30% of its time in the vinyl group. The same spin distribution was displayed in 2-vinylpyridine cation-radical. Surprisingly, an unpaired electron in 4-vinylpyridine cation-radical is held by the heterocyclic nitrogen atom, and not by the vinyl group. Both vinyl pyridine cation-radicals were generated under the same conditions (Eastland et al. 1984).

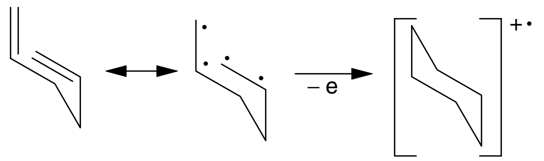
The cation-radicals of 1,3-dioxolane (i.e., of 1,3-dioxacylopentane), 1,3-dioxane (1,3-dioxacyclohexane), or 1,3,5-trioxane (1,3,5-trioxacyclohexane) were radiolytically generated in Freon matrix at 77 K. Their ESR spectra show an unusually strong splitting from protons of the OCH_2O group, namely, 15.3 mT in the case of the 1,3-dioxolane cation-radical. Interestingly, proton splitting for the 2-CH_2 group in the tetrahydrofuran cation-radical is equal to 8.9 mT only. According to the calculations and in agreement with ESR data, such 1,3-dioxa cation-radicals exist in half-boat conformations, with a π-spin density distributed between the two oxygen atoms separated by the methylene group. In other words, the splitting enhancement in the ESR spectra is explained with one-electron shift from (••O) atom to ($O^{+\bullet}$) parts through the CH_2 group (Snow et al. 1982, Symons and Wren 1984, Janovsky et al. 2003; see Scheme 2.42).

The conclusion on hyperconjugation in the OCH_2O fragment of 1,3-dioxolane cation-radical was also demonstrated by the mass spectrometry method (Todres et al. 1981). As calculated, the carbon–hydrogen bonds corresponding to OCH_2O in the cation-radical are weaker than those in the neutral molecule. Therefore, this site has to exhibit maximal probability of deprotonation with the formation of 2-yl radical. In experiments (Belevskii et al. 1998), photoirradiation of 1,3-dioxolane solutions in sulfur hexafluoride at 77 K leads to the formation of the cation-radical of 1,3-dioxolane and 1,3-dioxolan-2-yl radical. Consecutive ring opening, isomerization into linear products, and then ring closure reactions were registered by ESR method for this cation-radical (Baskakov et al. 2000).

X-ray irradiation of a matrix containing 2,6-difluorophenylazide in methylene chloride allows fixing the corresponding arylnitrene cation-radical, although such a particle is extremely unstable (Carra et al. 2006).

The following two examples concern organic anion-radicals. Radiolysis of 4-nitrobenzyl chloride or bromide (^{60}Co, MeTHF, at 77 K) leads to the formation of corresponding anion-radicals with no C–Hal cleavage (Symons and Bowman 1984). With methods of anion-radical generation in the liquid phase, attempts to fix in halonitrobenzyl anion-radicals were unsuccessful. Indeed, the glass technique allows one to record ESR spectra, observe splitting at nitrogen and halogen, and as a result, establish the principal ability of these anion-radicals to exist.

Monomolecular reactions of anion-radicals can be exemplified as follows. The acetylene anion-radical was successfully generated in a glassy MeTHF matrix by ionizing irradiation (^{60}Co) at 77 K. On illumination with a light of wavelength 430 nm, the following isomerization takes place (Itagaki and Shiotani 1999): $(CH{\equiv}CH)^{-\bullet} \rightarrow CH_2{=}C{:}^{-}$. When 3-methylpentane was used as a matrix molecule instead of MeTHF, however, no such isomerization reaction was observed. This could be due to the nature of 3-methylpentane, which gives a nonpolar and soft matrix. MeTHF is a polar molecule, which forms a rigid glassy matrix. The electrons generated by ionizing irradiation are stabilized in MeTHF. The polar and rigid nature of MeTHF matrix can be responsible for this phenomenon. Both anion-radicals are thermally stable, and therefore, the photoisomerization reaction noted was observed.



SCHEME 2.43

Ionization of 1,5-hexadiene in fluorochloroalkane matrix (Scheme 2.43) represents cation-radical monomolecular reactions. The initially formed cation-radical collapses to the cyclohexane cation-radical, that is, spontaneous cyclization takes place (Williams 1994). Zhu et al. (1998) pointed out that the ring formation from the excited valence isomer in the center of Scheme 2.43 is easier than in the corresponding ground-state dienes. Notably, tandem mass spectrometry revealed the same transformation of 1,5-hexadiene in the gas phase too. This provides us with a hint that mass spectrometry can serve as a method to express predictions of monomolecular transformation of cation-radicals in the condensed phase. A review by Lobodin and Lebedev (2005) discusses this possibility in more detail.

2.7.2 Organic Ion-Radical as Constituents of Solid Salts

The problem of preparation of pure ion-radical salts in solid state is very important technically. This problem is decisive in new application fields such as organic conductors, semiconductors, and magnets. Especially, Chapter 8 of this book considers methods for the preparation of solid ion-radical salts for these materials.

2.8 FORMATION AND BEHAVIOR OF ION-RADICALS WITHIN CONFINES

2.8.1 Micellar Media

Generation of organic ion-radicals is frequently complicated by diffusional separation of the reaction participants during the forward or back electron transfers. The problem can, however, be circumvented by using micellar media where diffusion of the reactants is largely retarded or prevented. The generation of organic ion-radicals often proceeds through the interaction between the donor and acceptor molecules. The interaction involves the formation of a donor–acceptor complex (encounter, then charge-transfer and then charge-separated complexes). The process eventually leads to a pair of free ion-radicals. Organized assembles such as micelles, reverse micelles, and vesicles prolong the lifetime of the charge-transfer states and thus increase the efficiency of charge separation by the charge partition in the intermediary complexes and the formation of ion-radical products.

Thus, perylene confined in an aqueous micelle containing cetylpyridinium chloride surfactant acquires a possibility to reduce the pyridinium headgroup of this surfactant in conditions of photoexcitation (Singh et al. 2005). The perylene molecule is localized at or near the micellar surface, where it coexists with the pyridinium moieties. Such a confinement promotes electron transfer. This process of electron transfer (forward transfer) proceeds in the ultrafast regime. Perylene transforms into the cation-radical (in its excited state). Because the cation-radical bears a positive charge, it is forced to leave the positively charged headgroup space and move into the neutral zone of the cetyl chains within the micelle. Accordingly, back electron transfer becomes less probable. The works by Okamoto et al. (2001) and Bharathy et al. (2005) showed how one could regulate ion-radical (nonphotochemical) reactions by the construction of cationic, anionic, or neutral micelles. Importantly, Okamoto's example (detailed in Section 4.5.4.4) shows that checking effects of diverse micelles allow elucidating the ion-radical mechanism of an organic reaction.

It should be noted that charged micelles create medium polarity, which is a very important factor for the ion-radical formation. The reaction of bilirubin with peroxy radicals is a prominent example. In biological systems, bilirubin acts as an antioxidant. It has also been claimed that it is a

"major physiologic antioxidant cytoprotectant" (Baranano et al. 2002). Hatfield and Barclay (2004) established that bilirubin shows very weak antioxidant activity in a nonpolar medium of styrene or cumene in chlorobenzene. In contrast, bilirubin exhibited strong antioxidant activity in aqueous sodium dodecylsulfate micelles, containing phosphate buffer (pH 7.4). At this pH, the pyrrol fragments of bilirubin keep their strong electron-donor ability. Reaction between bilirubin and peroxy radicals leads to the formation of bilirubun cation-radicals and peroxides. Peroxides are acceptors of protons, whereas bilirubin cation-radicals are very strong proton donors. Being generated in close contact, these electron-transfer products interact according to the proton-transfer scheme. The cation-radicals of bilirubin transform into pyrrole-centered radicals, and the peroxides turn into hydroperoxides. These transformations lead to the annihilation of peroxy radicals with their malignant ability. Such a result was observed in experiments where the micelles contained methyl linoleate. This ester is readily oxidized by peroxy radicals. The presence of bilirubin in the micelles inhibited the oxidation of methyl linoleate. It is the anionic character of the micelle that makes the described cation-radical mechanism possible.

2.8.2 Porous Media

Alkali metals are powerful reducing agents, which are often used to reduce organic compounds. However, because they react with air, their use requires precautions. Recently, new materials with essentially the same reducing power as the parent alkali metals were developed by intercalation of up to 40 mass% of liquid metal into nanopores of amorphous silica gel. These materials are non-pyrophoric and have good stability in dry air, making them easy to handle and store in desiccators. The sodium-containing material reduces biphenyl to anion-radical, for instance. Being included into the silica gel, the anion-radical acquires an enhanced stability. Dye et al. (2005) and Shatnawi et al. (2007; the production of the same research group) described the preparation and properties of alkali metals in silica gel nanopores.

The reaction of tetrathiafulvalene with silver nitrate provides a unique example where porous confinement is achieved in the reaction system itself in the absence of an alien porous material. Wang et al. (2003) monitored ultraviolet (UV) absorption of a colloidal dispersion of the reactants in AN. The intensity of the 436 nm band belonging to the tetrathiafulvalene cation-radical nitrate initially increased and reached a maximum of up to 152 h after mixing of the starting materials. After 504 h of aging, the band, however, completely disappeared. This period of aging corresponds to the formation of a large precipitate. A purple solid product was obtained by centrifugation. All the tetrathiafulvalene cation-radicals were incorporated into the silver precipitate. Transmission scanning electron microscopy or scanning electron micrography revealed that the precipitate had the structure of a snowflake dendrite with an average diameter of 2.8 μm. Wang et al. (2003) ascribe the formation of this well-defined silver dendritic nanostructure to the initial penetration of metallic silver into the interspaces of the resulting crystals of the silver salt of tetratiafulvalene cation-radical nitrate. Further, the silver particles are released one by one from sites arbitrarily far from a central cluster and stick irreversibly on first contact with the growing cluster. Because of their Brownian trajectories, which stimulate diffusion, the particles cannot penetrate deeply into a cluster without intercepting a cluster arm. The arms effectively screen the interior from the flux of incoming particles. Therefore, growth occurs preferentially at the exterior sites and the cation-radical salt occurs to be immured within the silver porous dendrite. The whole process is a good illustration of advantages of cation-radical formation in metallic nanotechnology.

Organic molecules spontaneously form corresponding cation-radicals on inclusion within activated zeolites (Yoon and Kochi 1988, Yoon 1993, Pitchumani et al. 1997). Zeolites are crystalline alumosilicate minerals that are widely used as sorbents, ion exchangers, catalysts, and catalyst supports. As zeolites act as electron acceptors due to the presence of Lewis- or Broensted-acid sites, confined organic compounds occur to be electron donors. Frequently, the interaction of electron donor with electron acceptor centers spontaneously generates cation-radicals and traps the ejected electrons.

Zeolites have a large free intracrystalline volume consisting of channels and cages of atomic dimensions, sometimes interconnected. The zeolite lattice consists of a three-dimensional network of tetrahedral $[SiO_4]^{4-}$ and $[AlO_4]^{5-}$ with Si or Al atoms at centers and O atoms in each corner. During trapping, electron migration can occur over the electron-deficient sites in the zeolite, such as sodium cations (e.g., in Na-ZSM-5) or aluminum centers. Alternatively, migration of the hole (redistribution of a positive charge) can occur via electron-rich sites, such as oxygen sites in the zeolite framework. Of course, the electron-donor ability of an organic compound is important for such a reaction. However, diverse zeolites differentiate in their acceptor power. The cation-radicals are formed along with carbocations, but the carbocation generation can be diminished by means of selection of an appropriate zeolite and activation manner. For instance, Ca(Y) zeolite activated at above 400°C on a high-vacuum line was found to be ideal for cation-radical generation when a diarylethene was sorbed from the cyclohexane solution. The generation proceeds even in the absence of light, with minimum interference from carbocations (Pitchumani et al. 1997).

Let us compare M-ZSM-5 zeolites with M = H^+, Li^+, Na^+, K^+, Rb^+, Cs^+, Al^{3+}, on one hand, and organic electron donors of variable ionization potentials, on the other. Zeolite H-ZSM-5 generates cation-radicals from substrates with an oxidation potential of up to 1.65 V (Ramamurthy et al. 1991). The naphthalene sorption by Al-ZSM-5 zeolites calcified in an atmosphere of oxygen or argon leads to the appearance of two occluded particles—the naphthalene cation-radical and isolated electron. Both particles were fixed by ESR method. Back reaction between the oppositely charged particles proceeds in an extremely slow manner and both the signals persist over several weeks at room temperature (Moissette et al. 2003).

Easily ionizable anthracene forms the cation-radical as a result of sorption within Li-ZSM-5. In case of other alkali cations, anthracene was sorbed within M-ZSM-5 as an intact molecule without ionization (Marquis et al. 2005). Among the counterbalancing alkali cations, only Li^+ can induce sufficient polarization energy to initiate spontaneous ionization during the anthracene sorption. The lithium cation has the smallest ion radius and its distance to the oxygen net is the shortest. The ejected electron appears to be delocalized in a restricted space around Li^+ ion and Al and Si atoms in the zeolite framework. The anthracene cation-radical appears to be in proximity to the space where the electron is delocalized. This opens a possibility for the anthracene cation-radical to be stabilized by the electron's negative field. In other words, a special driving force for one-electron transfer is formed, in case of Li-ZSM-5.

An important peculiarity of zeolites is their selectivity with respect to the substrate shape and conformation. The internal cavity system of a zeolite can host organic guest molecules. The type of guests sorbed depends on the chemical nature, dimensions, and topology of the zeolite channels and cages. For instance, the zeolite ZSM-5 is bidirectional because its internal space is constituted by two systems of oval channels—one straight (0.53 × 0.56 nm) and the other sinusoidal with an elliptical opening (0.51 × 0.55 nm)—crossing each other at right angles (Garcia and Roth 2002, Moissette et al. 2007). Accordingly, *trans*-1,2-diphenylcyclopropane is readily incorporated into the channels of Na-ZSM-5, whereas the cis counterpart remains unconfined (Herbertz et al. 2000). The trans isomer fits into the zeolite channel (whose internal diameter is approximately 0.55 nm), whereas the cis isomer appears too bulky. On reacting with the zeolite, the incorporated trans isomer undergoes, one after another, one-electron oxidation, deprotonation, and ring opening.

A tight fit of the organic substrate within the zeolite pores or channels is essential for generating long-lived cation-radicals. For instance, biphenyl is tightly fitted at the intersections between the straight and sinusoidal channels of Na-ZSM-5. When biphenyl is sublimed into this zeolite under vacuum and then photoirradiated, the cation-radical is formed. Its lifetime within the pore attains days, much longer than that in the AN solution. As discussed for *trans*-stilbene, the aluminum-rich Na-ZSM-5 zeolite promotes the generation of a very long electron–hole pair during photoexcitation. The lifetime of the pair exceeds several hours at room temperature. Disappearance of the stilbene cation-radical is preferentially caused by subsequent electron transfer from the electron-donor

oxygen atom of the zeolite framework to the electron-deficient stilbene cation-radical. The decay takes place slowly (Moissette et al. 2007).

Cation-radicals, stabilized in zeolites, are excellent one-electron oxidizers for alkenes. In this bimolecular reaction, only those oxidizable alkenes can give rise to cation-radicals, which are able to penetrate into the zeolite channels. From two dienes, 2,4-hexadiene and cyclooctadiene, only the linear one (with the cylindrical width of 0.44 nm) can reach the biphenyl cation-radical or encounter it in the channel (if the cation-radical migrates from its site toward the donor). The eight-membered ring is too large to penetrate into the Na-ZSM-5 channels. The cyclooctadiene can be confined if the cylindrical width is 0.61 nm, however the width of the channels in Na-ZSM-5 is only 0.55 nm. No cyclooctadiene reaction with the confined biphenyl cation-radical was detected despite the fact that, in solution, one-electron exchange between cyclooctadiene and $(\text{biphenyl})^{+\bullet}$ proceeds readily (Morkin et al. 2003).

The size compatibility is not the sole factor defining the very possibility of the cation-radical generation. Although the estimated width of 2,3-dihydrofuran is 0.38 nm, this cycloalkene ether does not react with biphenyl cation-radical confined in Na-ZSM-5 zeolite (in solution, this electron exchange proceeds easily). As Morkin et al. (2003) pointed out, it is possible that the preferred location of oxygen-containing dihydrofuran in zeolite is very different from that of 2,4-hexadiene. Particularly, the lone-pair electrons on the dihydrofuran oxygen can coordinate with the metal cations located on the external surface of zeolite. This inhibits the diffusion of dihydrofuran into the zeolite channels and prevents the possible electron exchange.

The restriction for a nucleophile to penetrate and react with the confined cation-radical sometimes leads to unexpected results. Comparing the reactions of thianthrene cation-radicals, Rangappa and Shine (2006) refer to the zeolite situation. When thianthrene is absorbed by zeolites, either by thermal evaporation or from solution, thianthrene cation-radical is formed. The adsorbed cation-radical is stable in zeolite for a very long time. If isooctane (2,2,4-trimethylpentane) was used as a solvent, *tert*-butylthianthrene was formed in high yield. The authors noted "it is apparent that the solvent underwent rupture, but the mechanism of the reaction remains unsolved."

Much needs to be done in this newly developing branch of ion-radical organic chemistry, which is still very intriguing.

2.8.3 Capsule Media

Encapsulation of organic ion-radicals markedly changes their chemical reactivity. It inhibits undesirable interactions and increases the desired properties due to shielding effects. Encapsulation is usually considered as host–guest or inclusion reactions.

For instance, inclusion of 1,1′-dimethyl-4,4′-dipyridyl cation-radical (the cation-radical of methyl viologen) into a cavity of sulfocalixarenes prevents the disadvantageous π dimerization. This is important for more effective use of viologens as components of electrochromic displays and electric conductors (Guo et al. 2007, references therein).

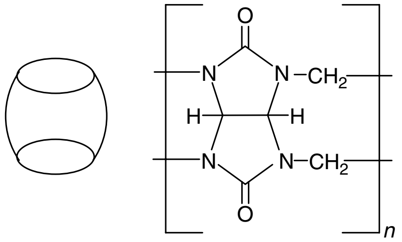
Cyclodextrin and cucurbituril are also interesting as hosts for the ion-radical guests. Cyclodextrins are conical, small barrel-shaped molecules consisting of D-glucose units with a fairly hydrophobic interior. The number of D-glucose units (6, 7, and 8 for α-, β-, and γ-cyclodextrin, respectively) defines the dimension of the host cavity and its possibility to include a guest. The nanocavity diameters and the internal volume range from 5 to 8 nm and 170 to 430 nm^3, respectively. Of course, a cavity size defines how deeply a guest can be inserted. This host–guest complexation, however, is governed by weak attractive forces. For a host–guest complex to exist, the size of the host must correspond to the diameter and volume of the cavity. In view of the wide variety of guest types, which can be inserted, there are diverse driving forces of inclusion reactions. And contributions to these forces also can widely vary. Particularly, van der Waals forces, hydrophobic/hydrophilic interaction, and release of strain energy are important. For instance, Tachikawa et al. (2005) studied one-electron oxidation of alkylaromatic sulfides, MeSAr. The substrates were inserted into hydroxypropyl β-cyclodextrin, HP-β-CD. The bromine anion-radicals ($Br_2^{-\bullet}$, generated by pulse radiolysis) acted

as one-electron oxidants. The bromine anion-radical is a strong oxidant and the redox potential of the $Br_2^{-\bullet}/2Br^-$ pair is 1.6 V against saturated calomel electrode (Neta et al. 1988). However, inhibition of one-electron oxidation was clearly observed when compared to the same process in the absence of HP-β-CD. Kinetics of MeSAr and $(MeSAr)^{+\bullet}$ exclusion from the HP-β-CD nanocavity was juxtaposed. As it turned out, the binding ability of $(MeSAr)^+$ with HP-β-CD occured to be much lower than that of MeSAr. In other words, inclusion forces of cyclodextrins are stronger with respect to neutral species rather than charged ones.

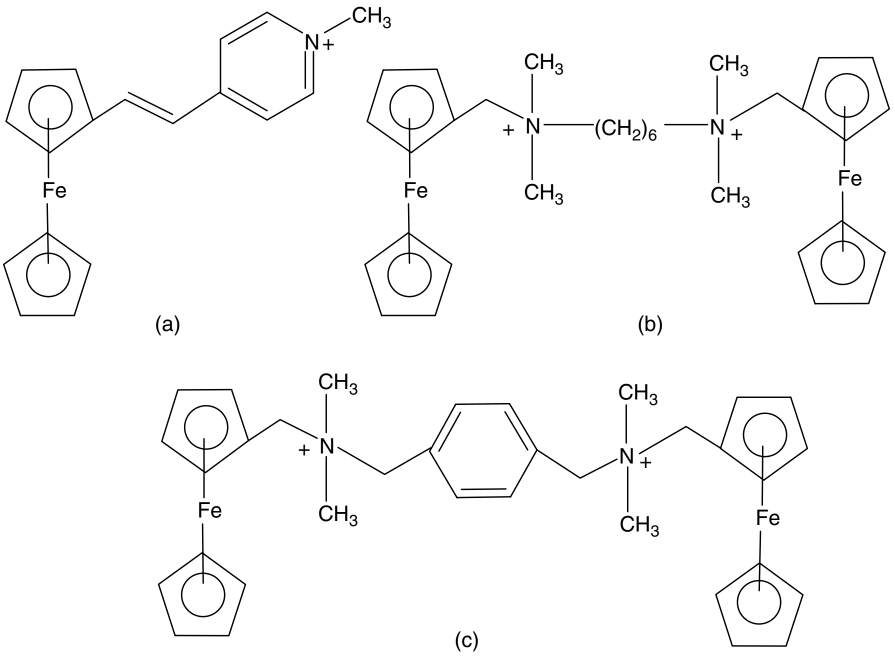
On the contrary, cucurbiturils preferentially confine *charged*, but not neutral, species. Cucurbiturils also possess cylindrical cavities suitable for the inclusion of organic molecules. Cucurbiturils are a family of macrocyclic host molecules consisting of methylene-bridged glucouril units (see Scheme 2.44).

Affinity of cucurbituril to cationic species is understandable because its cavity is formed from electron-rich carbonyl portals. This can be exemplified by a cationic species such as ferrocenylammonium derivatives depicted in Scheme 2.45.

The article by Kim et al. (2002) give an opportunity to compare the cations depicted in Scheme 2.45 and *N*,*N*′-dimethyl-4,4′-bipyridinium as guests to cucurbituril. The inclusion complex of *N*,*N*′-



SCHEME 2.44



SCHEME 2.45

dimethyl-4,4′-bipyridinium in cucurbituril is stable thermodynamically and kinetically. Electrochemical reduction study reveals that the host prefers the charged species, namely, dication and cation-radical, when compared to the doubly one-electron-reduced species . The ammonium derivatives shown in Scheme 2.45 contain ferrocenyl substituents that can be oxidized to ferrocenium ones. These derivatives were included into cucurbituril, which opens the possibility to study steric and polar effects on the oxidation of the confined cations caused by encapsulation. The first cation (structure a in Scheme 2.45) demonstrates steric selectivity of inclusion into cucurbituril. The positively charged (E)-1-ferrocenyl-2-(*N*-methylpyridinium-4-yl)ethylene forms a very stable inclusion complex. Only the trans isomer resides in the cavity referring to a small steric hindrance between carbonyl portals of curcubituril and this guest. The cis isomer is not acceptable due to steric hindrance (Wang et al. 2006).

Sobransingh and Kaifer (2006) installed *N*,*N*′-di(ferrocenylmethyl)-*N*,*N*′-dimethyl-1,6-hexylenyldiammonium or *N*,*N*′-di(ferrocenylmethyl)-*N*,*N*′-dimethyl-xylenyldiammonium (structures b and c in Scheme 2.45) in cucurbituril and performed electrochemical oxidation of the inclusion compounds. Oxidation transforms the ferrocenyl fragments to ferrocenium (cation-radical) moieties, that is, four-charged species are formed. It was established that curcubituril binds around the hexylenyl or xylylenyl diammonium units. This is seemingly caused by the attraction of the cavity to the two ammonium parts of these units whose positive charge densities are stronger than that of the two terminal ferrocenium moieties.

Besides Scheme 3.45, one more case of ferrocenylammonium oxidation deserves to be considered. That is, the chemical oxidation of the confined species. *N*-(ferrocenylmethylene)-*N*,*N*,*N*-trimethylammonium forms a remarkably stable inclusion complex with cucurbituril (Jeon et al. 2005). Yuan and Macartney (2007) used aqueous solution of the bis(2,6-pyridinedicarboxylato)cobaltate(III) ion for comparative oxidation of free and included compounds. This oxidant does not bind to curcubituril. As it turned out, the inclusion significantly reduces the rate constants for the ferrocenyl–ferroceniumly transition. One of the important causes of the retardation observed is the steric hindrance due to close approach of the oxidant to the encapsulated ferrocene (Yuan and Macartney 2007).

Of course, encapsulation can also be governed by other factors besides the charge control. Thus, the anion-radical of fullerene C_{60} exhibits better inclusion ability with cyclodextrins than neutral C_{60} (Liu et al. 2007). Polarizability of the anion-radical is much larger than that of neutral fullerene. This factor enhances dispersion forces and assists encapsulation of the charged particle by cyclodextrin.

To conclude this section, it is worth citing at least one example of ion-radical formation and transformation within crystalline charge-transfer complexes. It is known that the Diels–Alder reaction between 1,4-benzoquinone and 9,10-dimethylanthracene proceeds according to the ion-radical mechanism. Watanabe and Senna (2005) undertook an attempt to perform this reaction in the solid state, under vibrational milling. As it turned out, the reaction yield was relatively low when compared to the conventional solution reaction. However, the interaction of benzoquinone with dimethylanthracene under mechanical stressing resulted in the formation of cycloadduct with a quantitative yield when (*rac*)-1,1′-bis-(2-naphthol) was added to the reaction mixture. The effect of this additive is based on the formation of charge-transfer complex with strong hydrogen bonds. Using x-ray diffraction method, the authors established that bis(2-napthol) incorporates both quinone and dimethylanthracene, simultaneously. This provides a crystallographically ordered homogeneous reaction field and the cycloaddition proceeds smoothly and exhaustively.

2.9 CONCLUSION

Data on ion-radical formation show wide diversity of preparative methods. A variety of methods are available and the choice between them is still largely empirical.

Liquid-phase electron-transfer reactions that lead to the formation of ion-radicals can be reversible. The equilibria of these reactions can be managed to obtain the desired results. This chapter

considers methods of such management. Electrochemical methods of ion-radical generation in comparison with chemical ones are given. Chemically generated ion-radicals can exist in solutions or, in some special cases, as solids. The peculiarities of all the methods used for ion-radical generation are essential in the understanding of ion-radical reactivity.

In general, the experimental results presented emphasize some distinction between chemical and electrochemical electron-transfer reactions. At the same time, both kinds of reactions share a fair number of features. A greater combination of these two methods in the organic chemistry of ion-radicals would seem to be fruitful.

Isotope-containing organic compounds participate in electron-transfer reactions in a specific manner. This chapter gives a concise review of relevant data, especially concerning the enrichment of the isotopomer mixtures of organic compounds by means of their transformation into ion-radicals.

Confinement of ion-radicals considerably changes their reactivity. What is more important for practical applications is that the confinement increases the ion-radical stability. For instance, the cation-radicals of polyanilines (emeraldines) sharply enhance their thermodynamic and kinetic stabilities when they are formed encapsulated in cucurbituril (Eelkema et al. 2007). Emeraldines have electric conductivity as high as $1 \times 10^3\ \Omega^{-1} \cdot \mathrm{cm}^{-1}$ (Lee et al. 2006). Encapsulation of emeraldines does not affect their electric behavior but makes them much more attractive for microelectronics. This chapter underlines the importance of confined ion-radicals for diverse branches of nanotechnology. Nanotechnology as a new engineering field puts forward many demands, and many of which are addressed to ion-radical organic chemistry. We must satisfy these demands. Calm seas never make a skilful sailor.

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3 Electronic Structure–Reactivity Relationship in Ion-Radical Organic Chemistry

3.1 INTRODUCTION

Organic ion-radicals carry a charge and an unpaired electron. Their distribution along a molecular contour determines ion-radical reactivity. Therefore, it is important to elucidate the principles that control organic ion-radical reactivity. As already noted, the main energetic characteristics of ion-radicals are connected with the MOs occupied by one (unpaired) electron. These orbitals are also named SOMOs. For the ion-radicals formed from nonpolar or not so strong polar molecules, SOMO encompasses atoms of the molecular carcass with an unpaired electron and the charge is equally distributed. For the ion-radicals formed from molecules with a significant charge separation, an unpaired electron is still located on the SOMO, but the charge is not equally distributed within the carcass. In the latter case, other occupied MOs can respond to make the so-called uncoupled situation. In an extreme case, spin and charge can sometimes be completely scattered forming distonic ion-radicals. These ion-radicals are considered in Section 3.2.4.

When ion-radicals come out as reactants, they react with other radicals or abstract atoms from neutral molecules according to the substrate's positions of the highest spin density. With electrophiles or nucleophiles, ion-radicals react at the positions of the highest charge density. Generally, in terms of the ion-radical nature, the main distinction when compared to the parent neutral molecules is the presence of a single electron. The appearance of a charge is an attendant event. Both spin and charge distributions are discussed in the chapter.

This chapter considers ion-radicals with *detained* and *released* single electrons. Some ion-radicals contain fragment orbitals that suspend an unpaired electron preferentially. Other ion-radicals are characterized by the delocalization of an unpaired electron along orbitals, which encompass the whole molecular framework more or less evenly. This chapter considers the material, comprised from this point of view, using the terms *detained* and *released* electron. Such an abstraction helps us to analyze these two intrinsic features of organic ion-radical reactivity.

Section 3.2 includes an extensive discussion on the formation of odd-electron bonds, ion pairing, and the distonic stabilization of ion-radicals at the expense of separation between their spins and charges. Section 3.3 deals with ion-radicals from the class of even spin-charge distribution. This class occurred more frequently in scientific works of past decades. However, the reader will find newly developed manifestations of the principle of the "released" electron, concerning spread conjugation and the fates of ion-radical precursors with increased dimensionality.

It is obvious that any categorization tends to name the main trait of the phenomenon under consideration. This is useful. At the same time, the categorization need not be understood literally because each effect possesses multiple characteristics. However, it is impossible to study anything without even a minimal classification. In fact, investigations on the ion-radical electronic structure appear to be more developed than studies on their reactivity. Therefore, not every example considered here is supplied with the reactivity description. However, future accomplishments in studies on ion-radical reactions will be better understood in terms of the principles stated here.

Section 3.4 is devoted to organic ion-radical behavior in living organisms. Particularly, the consideration of an ion-radical mechanism of carcinogenesis reflects a point of view, which is new, and, in many respects, promising.

3.2 PRINCIPLE OF "DETAINED" ELECTRON THAT CONTROLS ION-RADICAL REACTIVITY

3.2.1 Frontier-Orbital Control

During an electron transfer, the acceptor places its LUMO at the electron disposal and the donor releases an electron that is located on its HOMO. These orbitals are frontier orbitals. In the corresponding ion-radicals, the distribution of an unpaired electron proceeds, naturally, under frontier-orbital control. This definitely reflects in the ion-radical reactivity and not always by a self-obvious manner. Let us concisely trace peculiarities of ion-radical fragmentation reactions that are very important in organic synthesis.

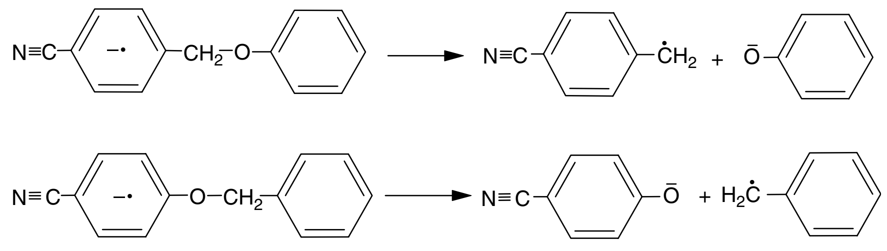
For instance, one-electron reduction provokes fragmentation of C—O bonds in cyanobenzyl alkyl ethers as shown in Scheme 3.1 (Pisano et al. 2002, Asensio et al. 2005). The anion-radical of cyanobenzyl phenyl ether fragments to phenolate and 4-cyanobenzyl radical, whereas the anion-radical of cyanophenyl benzyl ether gives 4-cyanophenolate and benzyl radical. This difference in fragmentation routes is understandable. The route that leads to the formation of the corresponding phenolate as the more stable particle is preferred. From the two developing phenolates, 4-cyanophenolate is, of course, more stable because of the direct polar conjugation between the electron donor hydroxylate and electron acceptor cyan groups. Nevertheless, the rate of the anion-radical of 4-cyanobenzyl phenyl ether fragmentation is higher than that of its isomeric counterpart. It is the specificity of the frontal orbital that causes this activation: The electron-withdrawing effect of the cyan group assists in the stabilization of the [$^{-\bullet}$N≡C—Ph—CH_2^{+-}O—Ph] transition state. Polarization of such a kind cannot be energetically advantageous for the [$^{-\bullet}$N≡C—Ph—$O^{-+}CH_2$—Ph] counterpart.

One-electron oxidation of *tert*-alkyl phenyl sulfides touches the sulfur atom. The sulfur-centered cation-radicals formed decompose, generating *tert*-alkylcarbonium ions and phenyl thiyl radicals. The cleavage direction completely corresponds to the spin–charge localization in the cation-radical: (Ph—$S^{+\bullet}$—CR_3) → Ph—$S^\bullet$ + $^+CR_3$. The fragmentation rate understandably depends on the stability of $^+CR_3$ leaving groups. Thus, the rate constants obey the following order: $Me_3C^+ < PhMe_2C^+ < Ph_2MeC^+ < Ph_3C^+$. The cleavage rate increases especially for (Ph—$S^{+\bullet}$—CPh_3). The presence of three phenyl groups at the *tert*-carbon atom determines a considerable steric crowding so that ($S^{+\bullet}$—CPh_3) bond cleavage is additionally favored by steric relief (Abboud et al. 2003, Baciocchi et al. 2006).

One-electron reduction of triorganyl sulfonium, selenonium, and telluronium salts ($R^1R^2R^3$ $Chalc^+$) proceeds according to the following sequence (Beak and Sullivan 1982, Eriksson et al. 2005):

$$R^1R^2R^3Chalc^+ + e \rightarrow R^1R^2R^3Chalc^\bullet \rightarrow R^1R^2Chalc + (R^3)^\bullet$$

Let us scrutinize this reaction on the example of phenyl dialkyl sulfonium salts. According to Saveant (2002), reductive cleavage of these salts obeys the stepwise mechanism. In other words,

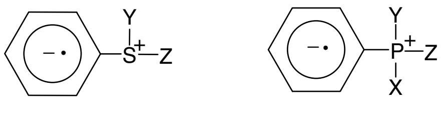


SCHEME 3.1

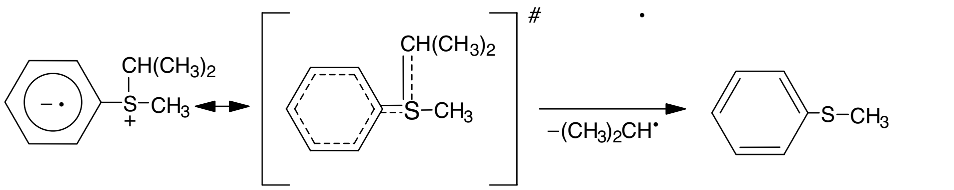
the reaction consists of the electron addition to the positive center of the salt followed by the stabilization of the sulfur-centered radical and the elimination of a carboradical. After that, a disubstituted sulfide is formed. Although this simple scheme corresponds to usual ideas, it cannot, however, explain many important features of the reaction. Although trialkyl sulfonium salts do not enter the reaction, phenyl dialkyl sulfonium salts, $PhR^2R^3S^+$, expel the bulkier alkyl on one-electron reduction. All these features can be explained by the intermediary formation of the so-called ligand π structures with localization of the charge and the electron arrived in the framework of the phenyl ring. Scheme 3.2 shows two examples of the ligand π structures for sulfonium (Beak and Sullivan 1982) and phosphonium salts (Hodgson and Coote 2005). Selenonium and telluronium salts belong to the same series (Eriksson et al. 2005).

In fact, electron transfer leads to the occupation of the frontal (vacant) orbital of an acceptor. This orbital must be vacant. This condition is necessary but insufficient. The energy level of LUMO must be low enough to provide a minimal gap between a LUMO level of the acceptor and a HOMO level of the donor. If the LUMO level is too high, the energy gap appears to be insurmountably wide. As mentioned earlier, trialkylsulfonium salts are not reduced. This means that they cannot provide a low-lying orbital for an entering electron although they bear a positive charge on the sulfur atom. In the case of the arylsulfonium salt, such a low-lying orbital is present. It is also obvious that this orbital is basically the aryl ring orbital. After the one-electron transfer onto the phenylmethylisopropyl sulfonium salt, its anion-radical is formed. The latter undergoes fragmentation giving an organic sulfide and a carboradical. A transition state, which leads to the fragmentation products, probably arises through overlapping of the phenyl- (which is populated by a single electron) and σ* orbital belonging to the bond that breaks homolytically. However, the bulkier alkyl group should be eliminated. The bulkier group has a stronger steric effect, which is reflected in the stronger elongation of the bond between this group and sulfur. This elongation results in the weakening of the bond. Besides, the bulkier group naturally goes into the plane that is perpendicular to the phenyl ring plane. This decreases steric stress and favors π−σ* conjugation. This type of conjugation is needed for the final stage of the reaction, which consists of the formation of arylalkyl sulfide and the capacious radical of another alkyl (see Scheme 3.3).

In the series of sulfonium salts with variable alkyl functions, the more stable radical is eliminated easily (Saeva and Morgan 1984). For instance, the *p*-cyanobenzyl radical separates more easily than the benzyl radical. (The shift of an unpaired electron in the phenyl ring is more effective when the cyano group is present in the para position.) Usually, the shift readability and inclination to reduction coincide; both the processes are interrelated. From this point of view, it is very interesting to juxtapose the *p*- and *m*-cyanobenzyl phenylmethyl sulfonium salts (Saeva and Morgan 1984). Under totally equal conditions, both salts are reduced at close electrode potentials, although the conjugated *p*-cyanobenzyl radical is principally much more stable than the nonconjugated meta



SCHEME 3.2



SCHEME 3.3

isomer. For the salts under comparison, both σ*-orbital energies of the bonds that would be disrupted are obviously close to each other. Clearly, this energy factor is more important than the difference in the stability of the eliminating radical, namely, p-$NCC_6H_4CH_2^{\bullet}$ and m-$NCC_6H_4CH_2^{\bullet}$.

The reaction of methoxy thioanisole with metallic sodium in hexaphosphotriamide initially results in the formation of the methoxy thioanisole anion-radical. SOMO in this anion-radical localizes much more at the thiomethyl group than at the methoxyl group. Scission of the thiomethyl group is the next step of the reaction. The obtained product is not reduced further.

$$Ar(OMe)SMe + Na \rightarrow Ar(OMe)SMe^{-\bullet}\,Na^{+} \rightarrow Ar(OMe)SNa + Me^{\bullet}$$

Strict selectivity of the reaction is explained by electroacceptor properties of sulfur *d* orbitals. These orbitals are not as high in energy as oxygen *d* orbitals are (Testaferi et al. 1982).

Anion-radicals of benzyl benzenesulfenate and *tert*-butyl benzenesulfenate prepared electrochemically undergo fragmentation at the expense of the sulfenate esterial group, but in a different mode. In the benzyl benzenesulfenate anion-radical, the S—O bond cleaves, whereas in the *tert*-butyl benzene sulfenate, the C—O bond splits (Stringle and Workentin 2005).

$$[PhSOCH_2Ph]^{-\bullet} \rightarrow PhS^{-} + {}^{\bullet}OCH_2Ph \text{ and } [PhSOC(CH_3)_3]^{-\bullet} \rightarrow PhSO^{-} + {}^{\bullet}C(CH_3)_3$$

The difference is explained with the variation in localization of the orbitals occupied by the excess electron, namely, over the S—O bond in the anion-radicals of benzyl benzenesulfenate ester and over the phenyl ring and S atom in the anion-radical of *tert*-butyl benzenesulfenate ester. Calculations within density functional theory show that the electron-donating capacity of the *tert*-butyl group increases the electron density on the O atom, shifting this orbital onto the aromatic ring, whereas the benzyl group has the opposite effect, decreasing the electron density at the O atom and drawing this orbital onto the S—O bond (Stringle and Workentin 2005).

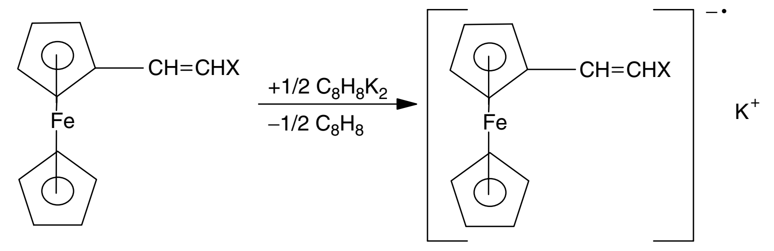
However, if a sulfur-containing group is conjugated with a stronger acceptor substituent, then this substituent, and not the sulfur-containing group, accepts an unpaired electron. This protects the sulfur-containing group from scission. For example, anion-radicals of benzene thiocyanates, sulfenamides, and alkyl esters of benzene sulfenic acid are not stable. They are cleaved to give diphenyl disulfides. The analogs with the nitro group in the ortho or para position of the benzene ring give stable anion-radicals with no scission in the enumerated sulfur-containing groups (Todres and Avagyan 1972, 1978).

Similarly, in anion-radicals of thioamides of nitrobenzoic acids, the nitro group prevails the thioamide group [$C(S)NR_2$] in competition for the unpaired electron (Ciureanu et al. 1987). Houmam et al. (2003) compared the behavior of benzyl thiocyanate and its 4-nitroderivative in conditions of electrolysis and cyclic voltammetry at a glassy electrode. Although benzyl thiocyanate eliminates cyanate, 4-nitrobenzylthiocyanate expels thiocyanate. The authors performed B3LYP calculations, which showed that frontier (LUMO) orbitals of both the depolarizers are different. The frontier orbital is spread over the benzylthiocyanate molecule but embraces the nitroaryl fragment in the 4-nitrobenzylthiocyanate counterpart. At the same time, C—SCN bond weakens. The cleavage generates two stabilized particles: 4-nitrobenzyl radical and thiocyanate anion.

If the nitro group is located at the ethylene fragment, one-electron transfer initiates dimerization of the developing anion-radicals. α-Nitrostilbene, ω-methyl-ω-nitrostyrene, and α-nitro-β-ferrocenylethylene give anion-radicals, which dimerize spontaneously. It is interesting to compare reactions of cyclooctatetraene dipotassium ($C_8H_8K_2$) with α-nitro and α-cyano ferrocenylethylenes (Todres and Tsvetkova 1987, Todres and Ermekov 1989; Scheme 3.4).

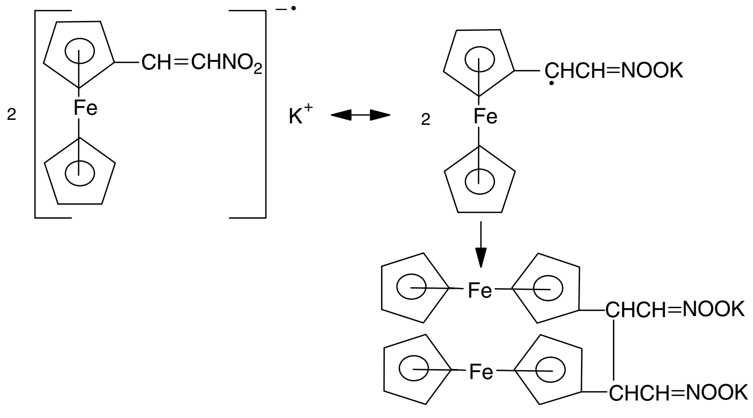
When X = CN, a stable anion-radical is obtained as evident from the ESR spectrum. When X = NO_2, the ESR signal cannot be observed. This anion-radical is unstable and gives rise to the dimer (isolated; Scheme 3.5).

It is interesting to note that reduction of cinnamonitrile, related to aromatic nitriles, gives dimers. Electrochemical dimerization of acrylonitrile is a well-known industrial process of the



X = CN, NO$_2$

SCHEME 3.4



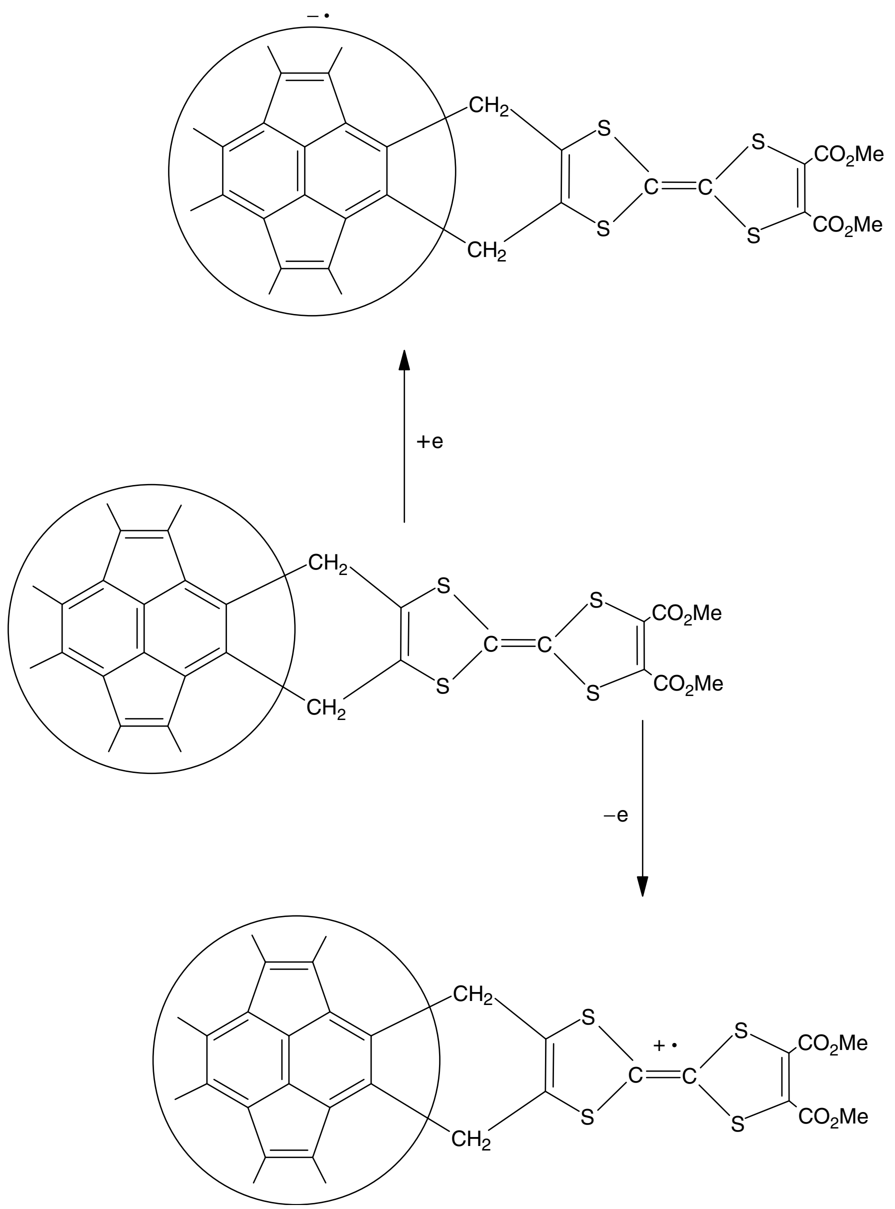
SCHEME 3.5

adipodinitrile manufacturing. Adipodinitrile is the starting material in the manufacture of nylon. The generation and dimerization of the acrylonitrile anion-radical proceed as follows:

$$2CH_2 = CHCN \xrightarrow{+2e} 2[CH_2 = CHCN]^{-\bullet} \leftrightarrow 2\dot{C}H_2\bar{C}HCN \xrightarrow{H^+} NC(CH_2)_4CN$$

In contrast to acrylonitrile and the related nitriles, ferrocenylacrylonitrile does not produce a dimer on one-electron reduction. Note that the ferrocenyl moiety is the common fragment of the nitro and cyano ferrocenylethylene anion-radicals. Hence, the shielding effect of the ferrocenyl group is evidently not the determining factor (in spite of a bulky size of the group). In the nitro group case, the ferrocenyl moiety cannot compete with the nitro group for an unpaired electron. The same situation was marked for the anion-radical of 1-cyano-4-nitrobenzene, where the nitro group appears to be "the main holder of the anionic charge" (Tsenov et al. 1998). In ferrocenylacrylonitrile, the ferrocenyl moiety can compete with the cyano group for an unpaired electron. The ability of the ferrocenyl group to participate in unpaired electron delocalization is documented (Todres et al. 1992). Competition between the ferrocenyl and cyano acceptors leads to strong delocalization of an unpaired electron throughout a molecular skeleton. This prevents dimerization of anion-radicals. Meanwhile, if an unpaired electron is suspended in the framework of the NOO$^-$ group, a radical center is formed at the β position, causing the mentioned dimerization.

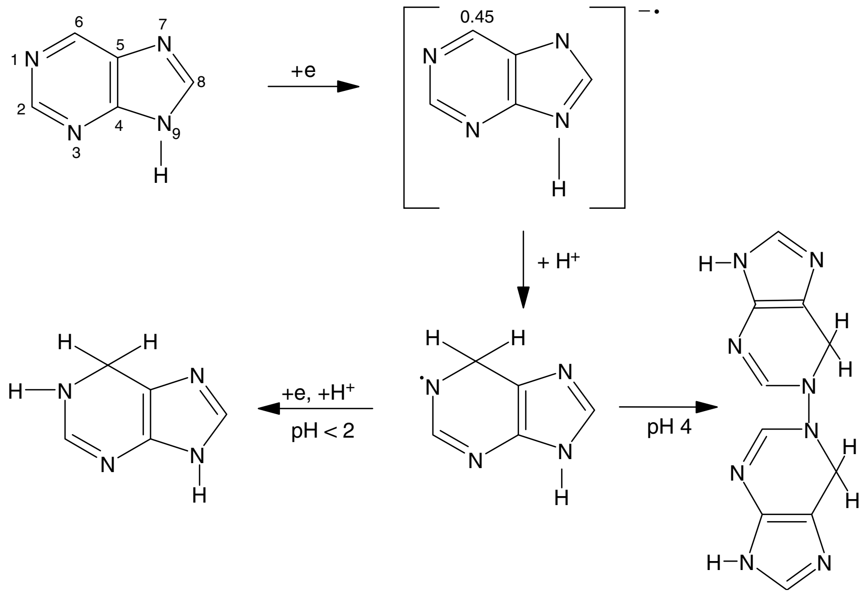
Adduct between C$_{60}$ fullerene and a tetrathiafulvalene derivative gives rise to ion-radicals with a very distinct difference between products of one-electron attachment and removal. This difference



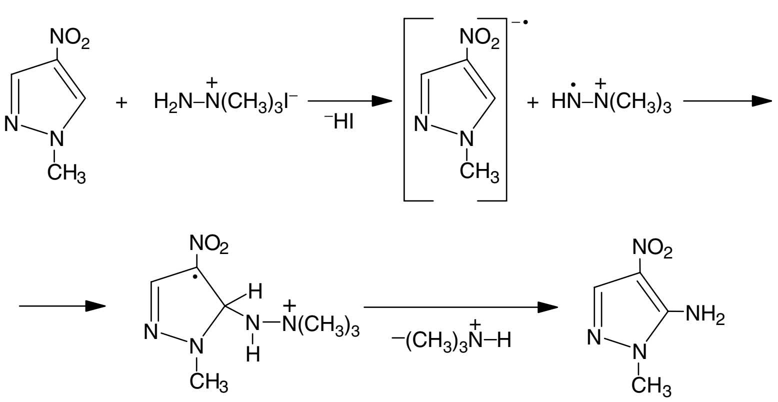
SCHEME 3.6

is seen in Scheme 3.6 (Llacay et al. 1998, Mas-Torrent et al. 2002). Such a distinction is very lucid because fullerene possesses pronounced electron acceptor properties, whereas tetrathiafulvalene is a pronounced electron donor. In terms of frontier orbitals, SOMO in the anion-radical belongs to the fullerene moiety, whereas SOMO in the cation-radical is localized within the fulvalene substituent.

Comparing electrochemical behavior and biological transformations of purine bases, Japanese chemists (Yao and Musha 1974, Ohya-Nishiguchi et al. 1980) have considered the anion-radicals of purine, its 8-deutero and 6,8-dideutero derivatives. As it turned out, up to 40% of the total spin density is localized in position 6 of the purine anion-radical (see Scheme 3.7). Ohya-Nishiguchi et al. (1980) noted that such a large localized spin density is very rare in a π electron system of the purine's size and should have important application in relation to its chemical reactivity. Protonation should



SCHEME 3.7



SCHEME 3.8

take place preferentially at position 6. This was deduced from the result of MO calculations (Nakajima and Pullman 1959). According to Fukui's frontier orbital theory (Fukui et al. 1952), such a reaction should take place at the position where the frontier electron density is the largest. The calculations clearly indicate that the large electron density is at position 6. Experimental data on protonation of the purine anion-radical is depicted in Scheme 3.7 (Yao and Musha 1974). Protonation indeed takes place at position 6. After that, the radical center appears at the cyclic nitrogen in the vicinal position 1.

The relationship between regioselectivity and the spin-density distribution is one of the very important indications that a definite reaction develops through the ion-radical mechanism. Such a relation was observed for the regioselective reaction between 1-methyl-4-nitropyrazole (substrate) and 1,1,1-trimethylhydrazinium iodide $[Me_3N^+NH_2I^-]$ in the presence of potassium *tert*-butylate in DMSO. Under these conditions, $[Me_3N^+NH_2I^-]$ transforms into $[Me_3N^+NH^-]$, which further acts as an electron donor. The first, rapid step consists of the formation of $[Me_3N^+NH^\bullet]$ particle and the 1-methyl-4-nitropyrazole anion-radical. The next, slow, step consists in the formation of σ complex as shown in Scheme 3.8. The complexation takes place in the solvent cage, but a part of the

anion-radicals escapes from the cage and is fixed by ESR method. In this anion-radical, the carbon atom at position 2 is enriched with the spin density ($\rho = -0.445$), whereas position 3 differs with a lack of the spin density ($\rho = +0.438$). The formation of the σ complex takes place when the terminal (spin-bearing) nitrogen atom of $[Me_3N^+NH^\bullet]$ particle is bound with the spin-deficient position 3 of the pyrazole ring. In the final product, the amino group appears to be exclusively in position 3 (see Scheme 3.8; Vakul'skaya et al. 2005).

The role of *t*-BuOK/DMSO mixture consists in deprotonation of the reactant to activate it for the reaction with the substrate, S, as shown in Scheme 3.9.

Scheme 3.8 represents a typical ion-radical mechanism of the so-called vicarious nucleophilic substitution of hydrogen as it was described by the pioneering chemist Mąkocza (Mąkocza 1989) in his summarizing review. ESR studies of other heterocyclic systems in conditions of the hydrogen-to-nucleophile vicarious substitution were reported by the research group at the Siberian branch of the Russian Academy of Sciences (Donskaya et al. 2002, Vakul'skaya et al. 2005, 2006, Titova et al. 2005).

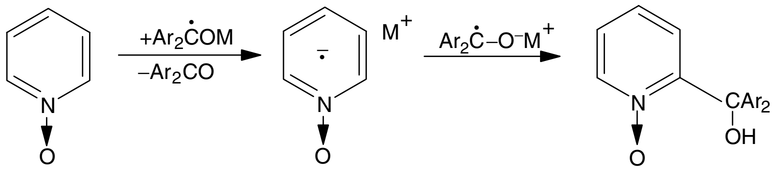
In the pyridine *N*-oxide anion-radical, the greatest spin density belongs to the carbon atom in the position 2 (Chaha 1986). In accordance with this, a reaction between the pyridine *N*-oxide anion-radical and the benzophenone metal ketyl yielded preferentially 2-diarylcarbinole derivatives (Kurbatova et al. 1980, Turaeva et al. 1993; Scheme 3.10).

The final product of Scheme 3.10 also forms as a result of the interaction between pyridine *N*-oxide in its neutral form and the double amount of benzophenone metal ketyl. Pyridine bases (not *N*-oxides) do not react with the ketyls. The *N*-oxides of pyridine and γ-picoline give both the *N*-oxide of the pyridyl carbinol and the pyridyl carbinol without the *N*-oxide oxygen. Yields can be 70 and 80%, respectively (depending on the metal nature in the metal ketyl). Having pronounced physiological activity, these compounds are the key materials in syntheses of atropinelike drugs. The reactions analogous to the one depicted in Scheme 3.10 have features that are generally significant in organic chemistry of anion-radicals. First, one-electron transfer from a reactant (the ketyl) to the substrate (the pyridine *N*-oxide) proceeds against the gradient of electrochemical potentials. Second, there is coupling of the two anion-radicals (which belong to different classes) despite charge repulsion. It follows that one-electron transfer can also take place at a nonfavorable (and not so high) difference between redox potentials if the transfer is reversible and one of the formed products goes out of equilibrium swiftly and irreversibly. Another conclusion is that dimerization of different anion-radicals can prevail over dimerization of identical anion-radicals when a "different ligand" dimer is promptly stabilized into a substitution product. The presence of a less thermodynamically stable but more reactive compound derived from the starting material makes a crucial contribution to the reaction.

$$H_2N\text{-}\overset{+}{N}(CH_3)_3I + t\text{-BuOK/DMSO} \longrightarrow KI + t\text{-BuOH/DMSO} + H\overset{-}{N}\text{-}\overset{+}{N}(CH_3)_3$$

$$H\overset{-}{N}\text{-}\overset{+}{N}(CH_3)_3 + S \longrightarrow S^{\bar{\bullet}} + (CH_3)_3\overset{+}{N}\text{-}\overset{\bullet}{N}H$$

SCHEME 3.9

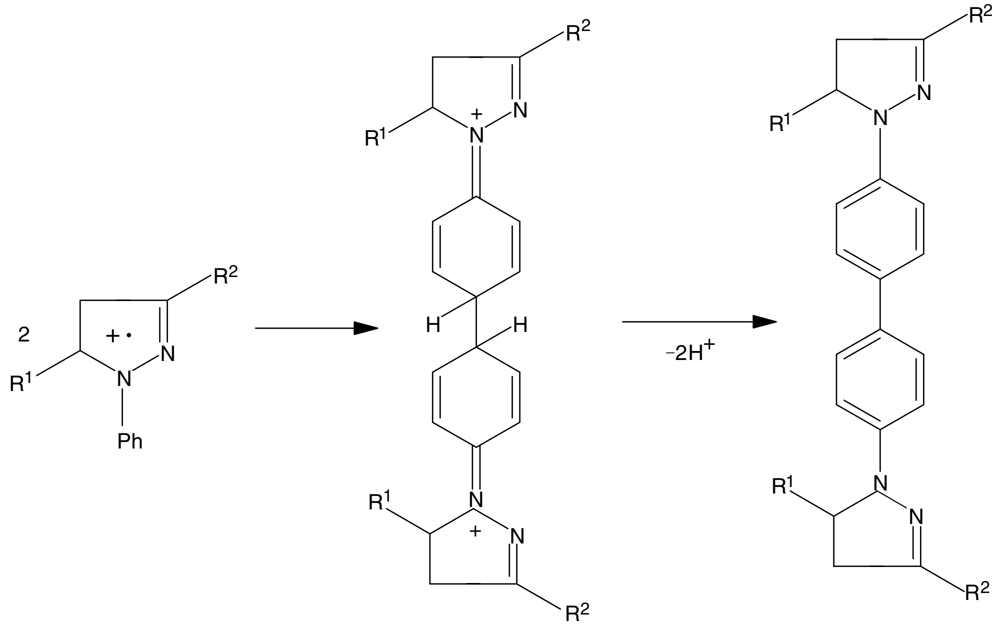


SCHEME 3.10

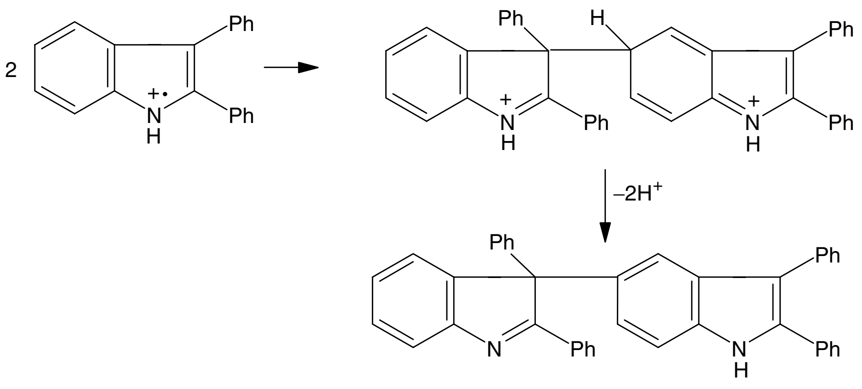
With respect to the aromatic *N*-oxide cation-radicals, one unusual feature of their behavior should be noted. After their development, they are prone to form dimers with a proton bridging the two *N*→*O* fragments of the two cation-radicals. Such structures are formed, for example, during the reactions between *N*-oxides of substituted quinolines and tetracyanoquinodimethide (TCNQ; Alekseeva et al. 1999). As it appears, the origin of a proton of the bridge deserves some additional study, perhaps by using deuterated participants. Probably, TCNQ, being a strong acceptor, is capable of abstracting electron from the donor—quinoline *N*-oxide. The latter, thus converts into a cation-radical, which takes up a hydrogen atom from the solvent (anhydrous acetonitrile) to form *N*-hydroxylquinolinium cation. It is the quinolinium cation that acts as a protonodonor for another *N*-oxide cation-radical from one of those that are still remaining in the solution. *N*-oxide cation-radicals were shown to abstract hydrogen even from alkanes (Geletii et al. 1986).

Coupling of identical ion-radicals seems to be the most effective way of preparing stereochemically identical dimers (Kise et al. 2001). Analyzing the dimer structure, one can distinguish a position of preferential localization of spin density. Thus, since the SOMO coefficient is greater at the α position than in the β position of the thiophene cation-radicals, only α,α′-coupling occurs. This is in accord with the experimental spin density distribution obtained from the ESR spectrum. Moreover, polymerization of the thiophene cation-radicals also proceeds at the expense of the α positions. The reaction leads to polythiophene. Polythiophene is of interest as a stable electrical conductor and semiconductor, especially when doped. This material is of value for "plastic electronics," in which lightweight, processable, and deformable plastics replace metals. There is a special review detailing properties of the oligothiophene cation-radicals (Glass 1999) as well as two principal original papers on the oligothiophene-dendron cation-radicals and the fullerene–oligothiophene–fullerene dumbbell cation-radicals (Apperloo et al. 2000).

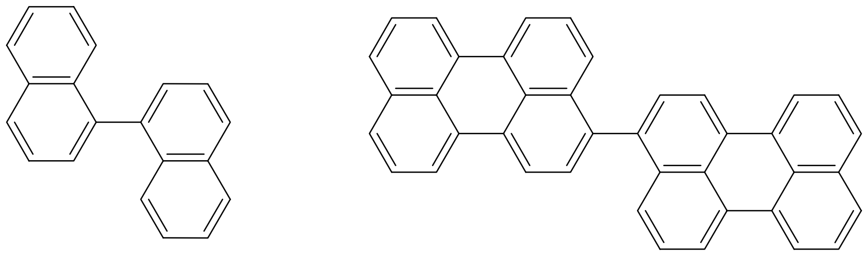
Dimerization of pyrazolines-2 on the action of oxidants includes the formation and doubling of cation-radicals (Morkovnik and Okhlobystin 1979). The doubling process is usually characterized by the terms *head* and *tail*. The term *head* is applicable to the position bearing a polar fragment, whereas the term *tail* is adopted for an unsaturated molecular site. The reaction under consideration follows the "head-to-head" order. This means that the doubling cation-radical has only a single position with the maximal density of an unpaired electron (Scheme 3.11).



SCHEME 3.11



SCHEME 3.12



SCHEME 3.13

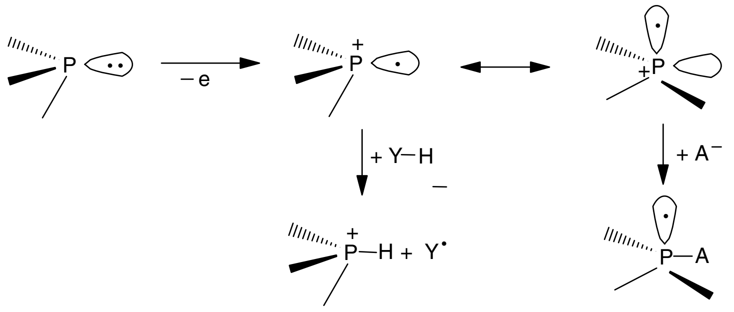
On the contrary, if just two positions in a cation-radical have the increased density of an unpaired electron, dimerization understandably follows a "head-to-tail" pattern. This is the case of 2,3-diphenyl indole (Check and Nelson 1978; Scheme 3.12).

The neutral molecules of 1,1′-binaphthyl and 1,1′-biperylenyl represent the classical case of atropoisomerism when one polycycle is under or above the other. A comparison between 1,1′-binaphthyl and 1,1′-biperylenyl in Scheme 3.13 shows their structural similarity.

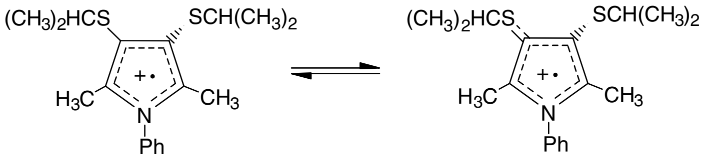
In the anion-radical form, 1,1′-binaphthyl acts as the single π system with a homogeneous spin distribution (Baumgarten et al. 1993). It is, therefore, somewhat surprising that in the 1,1′-biperylenyl anion-radical, Baumgarten et al. (1993) observed a localization of the unpaired electron in one moiety only, although the steric situation is anticipated to be similar to the one in 1,1′-binaphthyl anion-radical. This is explained by the fact that the atomic orbital coefficients of SOMO for the bridgehead positions are larger for binaphthyl anion-radical than for biperynyl anion-radical. Therefore, the interaction of the separate entities is more decoupled in the biperynyl case.

The possibility of orbital reorganization in ion-radicals should be taken into account. Thus, organic derivatives of three-valence phosphorus exist in the sp^3 hybrid state and an electron is removed from one of these orbitals. The cation-radical formed can retain the initial orbital configuration, but can also convert into the sp^3d hybrid state. In the latter case, one additional orbital of the phosphorus atom becomes accessible for the reactant attack. If Y—H bond in the reactant is weak, the reaction $R_3P^{+\bullet}$ + YH proceeds with the participation of an sp^3 frontal orbital according to the radical mechanism. Thiols are typical reactants with the weak Y—H bonds. If anions (A^-) react with $R_3P^{+\bullet}$, the vacant sp^3d orbital of the phosphorus appears to be a target. Scheme 3.14 illustrates the orbital pictures and the reaction directions.

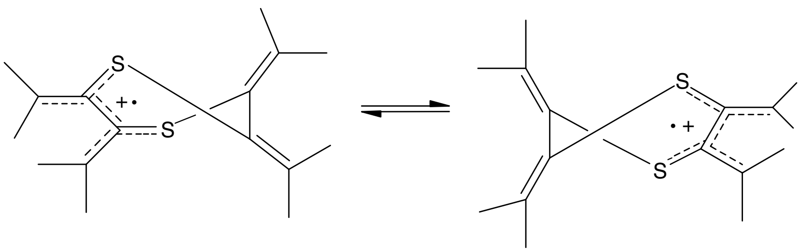
Scheme 3.14 is discussed as follows. Thiols react with the aliphatic phospine cation-radicals as hydrogen atom donors (Romakhin et al. 1995), but they come out as donors of thiolate anions,



SCHEME 3.14



SCHEME 3.15



SCHEME 3.16

reacting with the aromatic phosphine cation-radicals (Ohmori et al. 1980). This difference becomes understandable, if one takes into account the ability of the aromatic ring to delocalize an unpaired electron. Naturally, the aromatic phosphine cation-radicals expose less-defined radical properties than their aliphatic counterparts.

3.2.2 Steric Control over Spin Delocalization

A typical example of steric control over spin delocalization has been described for the cation-radical of 3,4-bis(thioisopropyl)-2,5-dimethyl-1-phenylpyrrole (Domingo et al. 2001). Scheme 3.15 depicts this situation. In this cation-radical, one thioisopropyl group is almost coplanar with the pyrrole ring, whereas the other one occupies an orthogonal position. Accordingly, the ESR spectra established an equilibrium between the symmetrical and asymmetrical conformations of the cation-radical. This equilibrium is shifted toward the asymmetrical form at low temperatures. The main feature of the equilibrium is the widening of spin delocalization, which includes not only the pyrrole ring but also one donor sulfur atom at the expense of the other sulfur atom. The steric control predetermines the discrimination of the other sulfur atom in the spin-delocalization process.

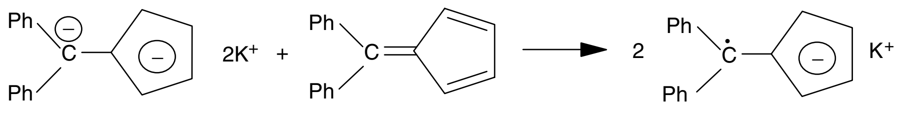
The cation-radical of permethyldithia[6]radialene provides one, even more pertinent, example of the steric control over spin delocalization (Gleiter et al. 1996). As described, the unpaired electron is delocalized only in one half of this cation-radical, namely, within the limits of the 2,3-dithiatetramethyl-butadiene unit. Owing to the steric demand of the isopropilidene groups, two of the four methylene groups are twisted, whereas the other two are coplanar (see Scheme 3.16). It seems

that this cation-radical belongs to the nonclassical type. (The classical/nonclassical designation was originally limited to carbocations, but is now used for cation-radicals too (see, for instance, Namai et al. 2007).

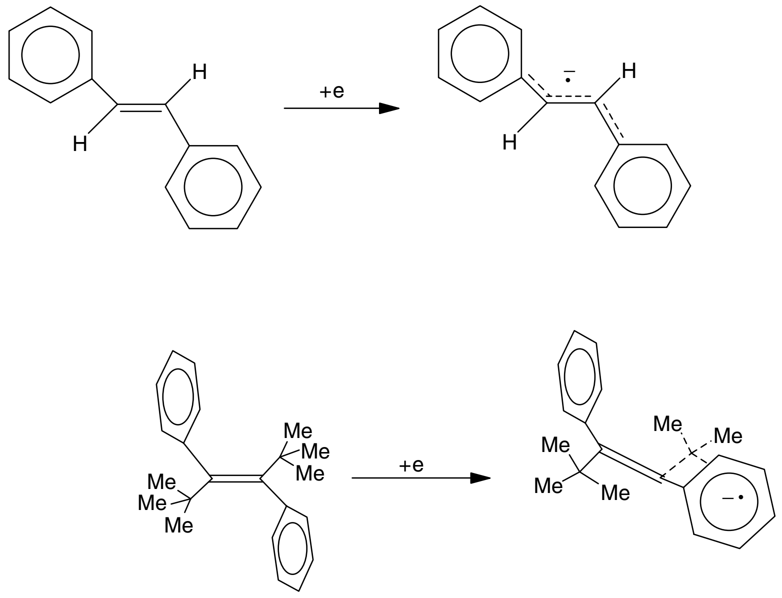
Diphenyl fulvene gives another example of steric control over spin delocalization in anion-radicals. The anion-radical is a result of reduction of diphenyl fulvene (Todres and Bespalov 1972) or oxidation of diphenyl cyclopentadienyl methane (Camaggi et al. 1971). The ESR spectrum of this anion-radical allows it to be viewed as a triarylmethyl radical in which one of the aryl groups is substituted by the anion of cyclopentadienyl (Camaggi et al. 1971). The radical center (the site of an unpaired electron) is shielded with two phenyl rings. The situation is similar to the one in triphenylmethyl radical, where stabilization of the radical center is secured with steric shielding and spin delocalization over and through phenyl rings. The cyclopentadienyl ring is stabilized like an aromatic anion. The anion-radical $Ph_2C^{\bullet}$—$C_5H_5^-$ is stable; it is not involved in dimerization or disproportionation and can be produced by the inverted reaction of the initially prepared dianion with the neutral molecule (Todres and Bespalov 1972; Scheme 3.17).

Hence, the anion-radical of diphenyl fulvene acquires a spin–charge distribution dictated by steric shielding at $Ph_2C^{\bullet}$ node and six-π-electron delocalization in the C_5H_5 ring. Anion-radicals of sterically congested stilbenes represent examples that are quite different, but at the same time are similar in principle. Let us compare the *E* structures of stilbene and its congested derivative, namely, α,β-di(*tert*-butyl)stilbene in their neutral and anion-radical forms (Scheme 3.18).

The *E*-stilbene molecule is planar in crystalline form, in gas phase, and presumably in solutions, although the phenyl group may be rotated as much as 32° to reduce nonbonded repulsions between hydrogen atoms (Waldek 1991, Meier 1992). This modest twisting still allows sufficient



SCHEME 3.17



SCHEME 3.18

π overlap for a continuous, conjugated π system between the phenyl groups and the central double bond. The introduction of two *tert*-butyl groups onto the central double bond in stilbene causes the phenyl groups to rotate out of the molecular plane so that their planes become perpendicular and their π systems become orthogonal to the central double bond (Gano et al. 1991, 1996). There is no conjugation between the phenyl groups through the ethylene π system.

In the anion-radical of stilbene itself (no substituents at the ethylenic bond), only moderate additional twisting about the central double bond takes place to retain much of the conjugation throughout the π system. The anion-radical of α,β-di(*tert*-butyl)stilbene appears to be more twisted when compared to the parent dibutylstilbene. In this anion-radical, the phenyl group and the adjacent carbon atom of the ethylenic bond form an autonomic benzyl-radical resembling fragment. This fragment just detains the unpaired electron and the accompanied negative charge in severance manner (Gano et al. 1996).

Another principal example is the anion-radical of 9,9′-bianthryl. In the neutral molecule of bianthryl, the anthracene units are arranged nearly orthogonally as it takes place in 1,1′-binaphthyl. But in contrast to binaphthyl, the orthogonal arrangement of the anthryl fragments remains in the anion-radical too: The unpaired electron is localized in one subunit. In this example, the conjugative interaction between two halves of the molecule is inhibited by the strong torsion about the connecting bond (Baumgarten et al. 1992).

To conclude, let us consider cation-radicals of hexaarylbenzene and its derivatives. The nearly perpendicular arrangement of the six planar aryl substituents relative to the central benzene ring forbids any through-bridge interaction between these tethered aryl groups (the central benzene ring is a bridge). When the aryl is *p*-(*N*,*N*-dialkylamino)phenyl, the corresponding cation-radical was isolated after the one-electron oxidation of the parent hexakis-substituted substance with dodecamethylcarboranyl radical. The resulting cation-radical was studied by the near-IR and ESR methods. The experiments brought sufficient proofs of spin migration by means of jumping from one *N*,*N*-(diaklylamino)phenyl fragment onto another one so that a closed ring current forms around the central benzene bridge. Spin delocalization through the central benzene ring does not take place. This electron hopping, in other words, peregrination, proceeds very fast forming a full donut-shaped toroid as aptly described by Rosokha et al. (2006).

3.2.3 Unpaired Electron Localization in the Field of Two or More Atoms

This section is devoted to odd-electron multicenter bonds. Two-center three-electron bonds were described by Pauling (1931). Since the first prediction by Pauling, a great deal of interest has been expressed in such systems. The following text provides a list of important references.

Clark (1988) calculated the stabilities of diverse species with odd-electron σ bonds. Cataldo et al. (2001) produced evidence for the existence of the anion-radical with an intramolecular one-electron bond between two phosphorus atoms in a macrocyclic structure of the metacyclophane type. Dutan et al. (2003) observed a similar situation for the anion-radical of a di (*m*-silylphenylenedisiloxane) analog.

Hoefelmeyer and Gabai (2000) have synthesized 1,8-bis(diphenylboryl)naphthalene and compared structures of this molecule and the anion-radical prepared from it. In the parent neutral molecule, the two boron centers occupy the peri position in the 1,8-disubstituted naphthalene. These neighboring boron centers are separated by a distance of 0.3 nm. In the anion-radical, the boron–boron distance appears to be approximately 0.1 nm longer than what is usual for compounds with single bonds between four-coordinated boron atoms. According to the ESR spectrum of the anion-radical discussed, the unpaired electron is preferentially suspended in the field of the two boron atoms. The one-electron σ bond emerges! This one-electron σ bond can obviously be viewed as resulting from the overlap of the formerly vacant and parallel *p* orbitals of two peri-located boron atoms. In the anion-radical, both the boron fragment orbitals are simultaneously populated with the unpaired electron.

Anion-radicals of alkylphenyldiazirines have been prepared electrochemically (Elson et al. 1986). Their ESR spectra show that the anion-radicals persistently hold the intact diazirine rings. A large portion of the spin density resides on the nitrogen atoms. In the three-membered diazirine ring, the sp^3 carbon atom is bound with two nitrogen atoms having a double bond between them. Hence, some kind of valence shell expansion takes place. The phenomenon developed, however, is in agreement with the simple valence bond picture of the molecules. In general, the azo group is considered as a fairly good electron acceptor favorable for the accommodation of the negative charge in anion-radicals (Gerson et al. 1996).

Apparently, a similar valence bond picture holds true for 4-alkylidene pyrazoline anion-radicals prepared by reducing of the pyrazolines depicted in Scheme 3.19.

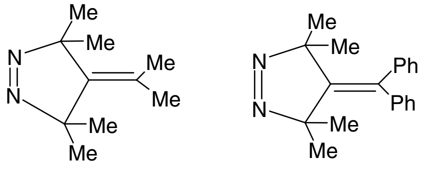
According to ESR spectra and MO calculations for these anion-radicals, the unpaired electron is indeed associated with the nitrogen–nitrogen π^* orbital (Bushby and Ng 1996).

Anion-radicals of compounds with the azo and diphosphene central bonds ($R^1N{=}NR^2$ and $R^1P{=}PR^2$) have three π electrons between two nitrogen or phosphorus atoms (Stagko et al. 1998, Binder et al. 1996, Shah et al. 1997).

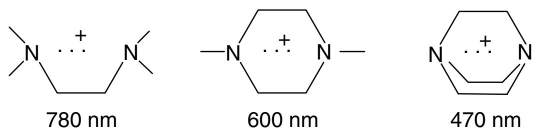
Gebicki's group compared absorption spectra of the cation-radicals of *N*,*N*′-dimethylethane diamine, *N*,*N*′-dimethylpiperazine, and hexamethylene diamine (Scheme 3.20) with cation-radicals of other α,ω-alkyldiamines (Gebicki et al. 1990, Marcinek et al. 1990). The absorption spectra of diamine cation-radicals with three or fewer methylene groups separating the nitrogen atoms show a visible transition, in contrast to those with four and six methylene groups, where only UV transition is seen. As the length of the polymethylene chain increases, the probability of achieving the conformation favorable for the $(N{\therefore}N)^+$ bond formation decreases sharply. Hence, the cation-radicals generated from α,ω-diaminobutane or α,ω-diaminohexane possess a charge localized only on one of the two nitrogen atoms, similar to monoamine cation-radicals.

One-electron oxidation of 1,6-diazabicyclo[4.4.4]tetradecane proceeds at a remarkably low rate. The cation-radical obtained contains a three-electron σ bond between the two nitrogen atoms (Alder and Sessions 1979). In this case, the three-electron bond links the two nitrogens that are disjoined in the initial neutral molecule, at the expense of one electron from the lone electron pair of the first nitrogen and the two electrons of the second nitrogen, which lasts as if it is unchangeable. The authors named such a phenomenon as "strong inward pyramidalization of the nitrogens" with "remarkable flexibility for the N–N interaction." This interaction results in $2\sigma{-}1\sigma^*$ bond formation (Scheme 3.21).

Such "strong inward pyramidalization of the nitrogen atoms" is stabilized by the overlapping of the nitrogen electrons forming a three-electron two-center bond in the cation-radical discussed in



SCHEME 3.19

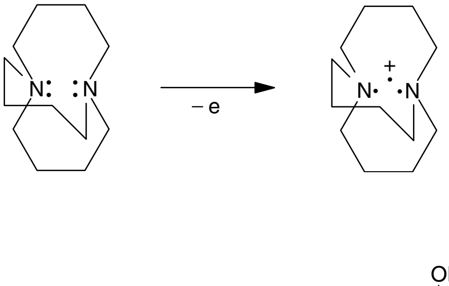


SCHEME 3.20

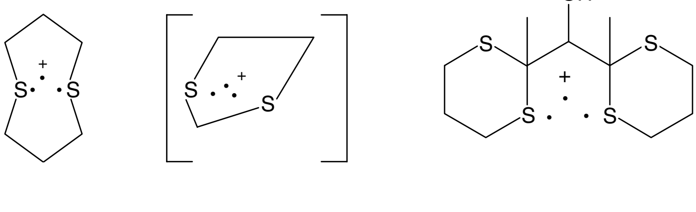
Scheme 3.21 (Zwier et al. 2001). The initial neutral compound shown in Scheme 3.21 is very sensitive to air as a solid and is stable only for a few hours. The fluoroborate salt of the 1,6-diazabicyclo[4.4.4] tetradecane cation-radical can be isolated as a dark red solid. The solid is indefinitely stable and in the absence of a base is stable for months in organic or even aqueous solutions(Alder and Sessions 1979). Three-electron N—N bound cation-radicals are known in a wide range of structures. Most examples are, however, unstable outside the glassy or solid state (for a review, see Alder 1983). The tricyclic cation-radical portrayed in Scheme 3.21 is structurally protected from the $(N \therefore N)^+$ bond being cleaved. This protection provides it a long solution lifetime (Nelsen et al. 1980).

Transannular cation-radicals with the intramolecular sulfur–sulfur bond of the 2σ–1σ* type generated from medium-ring disulfides such as 1,5-dithiacyclooctane are an exception in terms of their stability, although they are not resistant to water (Musker 1980). ESR and resonance Raman spectroscopy studies revealed the existence of the 1,5-dithiacyclooctane cation-radical, with substantial bonding between the sulfur atoms (Brown et al. 1981, Tamaoki et al. 1989). Computations confirmed this statement and pointed out that the chair–boat conformer has the lowest energy when compared to other possible conformers (Stowasser et al. 1999). Feldman's group compared experiments and computed data on cation-radicals of six-membered cycles containing two N, O, and S heteroatoms in positions 1 and 4, namely, the data on the cation-radicals of piperazine, morpholine, thiomorpholine, thioxane, and dithiane. Only in the dithiane case, the authors fixed the formation of a three-electron bond between the heteroatoms, that is, $S \therefore S$ bond. Only the dithiane cation-radical is situated in the boat conformation that makes such a transannular interaction possible. All of the other cation-radicals from this series exist in chair conformations and cannot form the corresponding three-electron bonds (Nuzhdin et al. 2005). In these "other" cases, the heteroatoms significantly differ in their electronegativity and such a difference plays an essential role.

The molecular geometry, which allows optimal *p* orbital interaction to yield a three-electron bond, presumes an orientation of *p* orbitals belonging to each sulfur atom along the $S \cdots S$ axis. This is the case of the chair–boat conformer of the 1,5-dithiacyclooctane cation-radical, the first structure in Scheme 3.22.In the 1,3-dithiacyclopentane cation-radical, the sulfur *p* orbitals are aligned almost perpendicular to the ring plane, and this prevents stabilization by the transannular interaction between the two sulfur atoms in the cycle. This unreal structure (the second structure in brackets in Scheme 3.22) cannot exist. However, the cation-radical of bis(2-methyl-1,3-dithianyl)methanol (the third structure in Scheme 3.22) was predicted to exist: Li and Kutateladze (2003) calculated this structure as the most stable because it differs by a special orbital pattern from the structure in brackets.

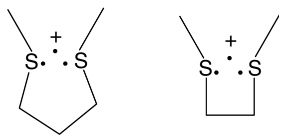


SCHEME 3.21



SCHEME 3.22

The open-chain compounds $-S-(CH_2)_n-S-$, $-Se-(CH_2)_n-Se-$, and $-S-(CH_2)_n-Se-$ give cation-radicals on one-electron oxidation. When n ranges from 3 to 5, these open-chain species exist in a form that has the three-electron two-center bonds(Mueller and Heinze 1998a, 1998b). Two of such forms are depicted in Scheme 3.23. Although the 2,6-dithiaheptane cation-radical can assume a five-member ring configuration and give a more or less stable three-electron bond, the cation-radical of 2,5-dithiahexane cannot overcome inner steric strains (Asmus 1979, Drewello et al. 1989). Therefore, such quasifused dithiacyclobutane cation-radical cannot be formed.



SCHEME 3.23

It should be noted, however, that the bond strength of the three-electron sulfur–sulfur bond is inevitably lower than that of a normal sulfur–sulfur bond in an organic disulfide. The theoretical results indicate that the bond is localized between the two sulfur atoms, both sulfur atoms have an equal unpaired electron density, and the S∴S bond length is about 30% longer than average length of S—S single bond. The bond strength is about 45% of the S—S single-bond energy. The bond order is 1/2 (James et al. 1996, Refs 2–5 therein). Cation-radicals containing such 2σ—1σ* bonds are unexpectedly ready for one-electron oxidation. In these cation-radicals, a p orbital of the sulfur atoms combines in a σ fashion to generate σ bonding and σ*-antibonding orbitals (Baird 1977, Gill and Radom 1988). Two electrons are accommodated in the σ-bonding MO (2σ) and one electron in the σ*-antibonding MO (1σ*). The electron to be removed from the cation-radical on oxidation is of course the antibonding σ* electron. In this case, only an increase in the bonding between the sulfur atoms can take place. For example, the cation-radical 1,5-dithiacyclooctane shown in Scheme 3.22 undergoes oxidation in AN at a potential less positive than that for 1,5-dithiacyclooctane itself: The neutral 1,5-dithiacyclooctane undergoes the two-electron oxidation, which proceeds reversibly in the framework of a merged process (Wilson et al. 1979, Ryan et al. 1981).

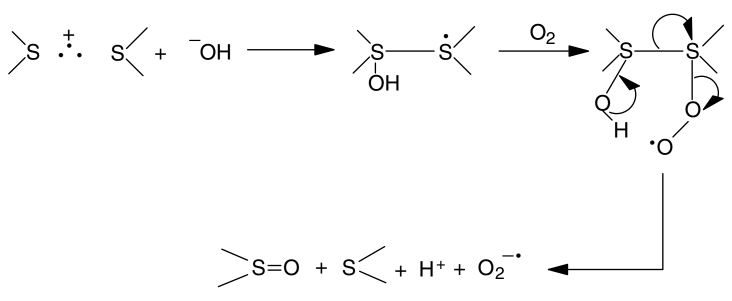
It is interesting to compare the S∴S and Se∴Se cation-radicals in terms of odd-electron binding. The former have already been exemplified here, the latter also exist. For instance, both thiourea and selenourea give three-electron bound cation-radicals, the dimer cation-radicals, on oxidation (Priyadarsini et al. 2005). In general, oxidation of selenium requires considerably less energy than oxidation of sulfur. This means that Se∴Se species are thermodynamically more stable than their S∴S analogs. Nevertheless, Se∴Se species are readily oxidized to the corresponding dications. For example (Asmus 2000),

$$(Me_2Se\therefore SeMe_2)^+ + Fe^{III}(CN)_6^{3-} \rightarrow Fe^{II}(CN)_6^{4-} + (Me_2Se{-}SeMe_2)^{2+}$$

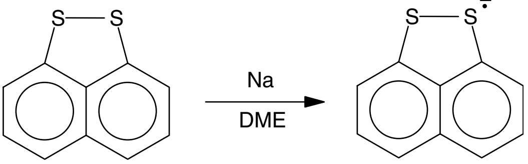
As for 2σ—1σ* dithia cation-radicals, they do not react directly with O_2. Aliphatic thioether cation-radicals as shown in Scheme 3.24 become capable of reacting with O_2 only after the addition of hydroxyl anion (Schoeneich et al. 1993).

At this point, it is to be noted that even when carbon–oxygen bonds are formed by a reaction of an olefin cation-radical with O_2, the reaction is rapidly reversible and endothermic (Nelsen 1987). Structures of observable products depend on the rate of reactions other than the interaction with O_2. This does not mean that adducts do not form, but that the R^+-$OO^•$ product is thermodynamically unstable. The same should be taken into account for 2σ—1σ* dithia cation-radicals.

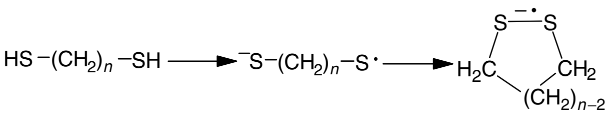
There are three possible types of three-electron bonds. Oxidation of a π bond leads to a cation-radical with σ, π three-electron bond. This bond contains no antibonding electrons, and the total bond strength exceeds that of a double bond by the energy of half a π bond. Olefins can acquire the 2σ—1π bond on one-electron oxidation, the bond constructed from the electrons 2σ and 1π. Oxidation of organic disulfides, RSSR, to their cation-radicals $(RSSR)^{+•}$ yields species in which the unpaired electron from the oxidized sulfur interacts with the unbound p-electron pair of the second sulfur (Glass 1999). This establishes a 2π—1π* bond *on top of the already existing σ bond.* The overall bond strength of this five-electron (2σ—2π—1π*) bond also exceeds that of the normal



SCHEME 3.24



SCHEME 3.25



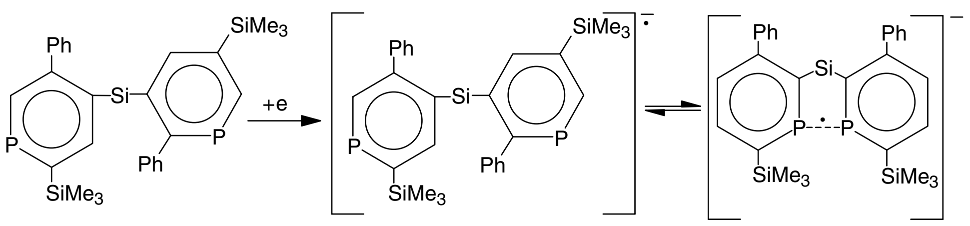
SCHEME 3.26

2*s* bond by approximately half of a π bond. In other words, the $(RSSR)^{+\bullet}$ assumes a partial π character. The 2σ–1σ* bond (with a formal bond order of 0.5) is formed from two electrons located in a σ orbital and one electron in an antibonding σ* orbital when there is no σ *bond between the atoms* participating in the formation of 2σ–1σ* bond. In contrast to $(CH_3SSCH_3)^{+\bullet}$, the 2σ–1σ* species $[(CH_3)_2S\therefore S(CH_3)_2]^{+\bullet}$ undergoes a rearrangement in which a C–C bond is formed (Goslish et al. 1985). The rearrangement includes α deprotonation at one of the $(CH_3)_2S$ fragments and the formation of an ilyde containing a $[-^{+}S(CH_3)CH_2-]$ fragment. Further regrouping leads to the formation of the SCH_2CH_3 moiety (Glass 1999).

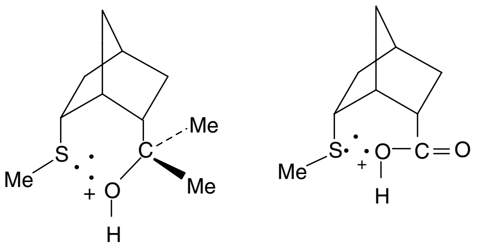
The well-known instability of the disulfide anion-radicals, $(R^1SSR^2)^{-\bullet}$, is apparently explained by the antibonding electron population, presumably in the framework of the disulfide bond. In some cases, these anion-radicals turned out to be more or less stable (Breitzer et al. 2001). Two examples are shown in Schemes 3.25 and 3.26 that needs to be distinguished. First, one-electron reduction of naphthalene-1,8-disulfide generates the corresponding anion-radical (Scheme 3.25).

Second, the oxidation of a [1,*n*]-dithiol by Ti(III)-H_2O_2 at pH 7 produces the cyclic disulfide as shown in Scheme 3.26. The final product of the dithiol oxidation forms a rather stable anion-radical.

There are two possible locations for the unpaired electron: Either it resides in a sulfur 3d orbital or it resides in the S–S σ^*_{3p} antibonding orbital. Considering ESR spectra of cyclic disulfide anion-radicals, Bassindale and Iley (1990) note that the orbital containing the unpaired electron has a *p* character almost entirely. In particular, the naphthalene-1,8-disulfide (peri-disulfide) anion-radical of Scheme 3.25 has an unpaired electron that is highly localized on sulfur, with little interaction between this electron and the π system of the aryl rings. Although this is in accord with a σ* orbital, *d* orbital participation would be expected to interact strongly with the π system and can, therefore, be ruled out. Disulfide anion-radicals ought to be considered species of 2σ–1σ* type.



SCHEME 3.27



SCHEME 3.28

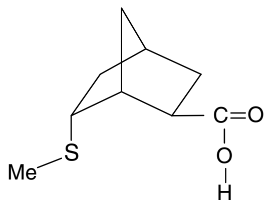
Scheme 3.27 represents a case when the odd-bond formation governs the geometry of an anion-radical (Choua et al. 2004). The substrate was reduced on an alkali mirror in the presence of a cryptand, giving the anion-radical, which is not coordinated to the counterion. Such a species undergoes internal rotation to adopt a conformation in which the two phosphine rings occur to be bound with a weak but real one-electron bond.

Let us now consider the formation of three-electron bonds between dissimilar atoms. Stabilization of an oxidized sulfur atom can, in principle, be achieved during its interaction with other heteroatoms if they provide free, preferably *p*-, electron pairs. Nitrogen, oxygen, and halogens (except fluorine) can be mentioned as such heteroatoms (Anklam et al. 1988, Carmichael 1997, Bobrowski et al. 2007). Stability of these bonds is generally not as high as that of a symmetric S∴S system. Owing to the difference in electronegativity, electron density is distributed unequally between two diverse heteroatoms. The bond strength for such a bond depends on the difference between ionization potentials (IPs) of these two atoms: The smaller the difference, the stronger the bond. In other words, the following sulfur neighbors are capable of forming three-electron bonds: Oxygen of the hydroxyl or carboxylate group, nitrogen of the amino group, and phosphorus of various phosphine moieties (Glass 1995). Scheme 3.28 represents two structures with more or less stable cation-radicals with three-electron bonds.

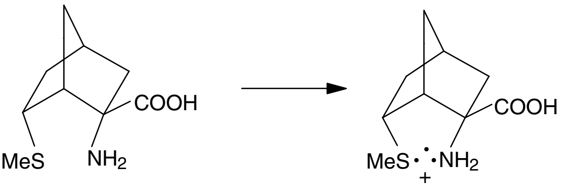
The cation-radicals depicted in Scheme 3.28 form on oxidation of *endo*-2-(2-hydroxy-2-methylethyl)-*endo*-6-(methylthio)-bicyclo[2.2.1]heptane and *endo*-2-(carboxyl)-*endo*-6-(methylthio)-bicyclo[2.2.1]heptane, respectively. Asmus (1990) underlined that only the sulfur atom responds to the one-electron oxidation. This is understandable since sulfur is less electronegative than oxygen. Meanwhile, the onium state is more stable than the sulfonium one.

When geometric constrains preclude the participation of a neighboring group, the three-electron bond is not formed. Scheme 3.29 gives one such example, namely, *exo*-2-(carboxy)-*endo*-6-(methylthio)-bicyclo[2.2.1]heptane.

Scheme 3.30 depicts an intriguing case, when one-electron oxidation of the conformationally constrained *exo*-2-(carboxy)-*endo*-2-(amino)-*endo*-6-(methylthio)-bicyclo[2.2.1]heptane gives rise to a cation-radical in which an amino- and not a carboxylate group participates in the three-electron bond with sulfur (Glass 1995).



SCHEME 3.29



SCHEME 3.30

In sulfenamides ($R^1S{-}NR^2R^3$), the cation-radicals keep an unpaired electron occupying a π* orbital. This orbital is localized between the sulfur and nitrogen atoms. As a matter of fact, a slight S=N double bond character exists in the neutral sulfenamides. A consequence of this "double bond" character is an increase in the energy barrier, which restricts rotation around the S–N bond. Restricted rotation about the S–N bond is known in neutral sulfenamides (Kost and Raban 1990). Notably, the energy barrier to this rotation is greater for the derived cation-radicals when compared to the parent compounds (Bassindale and Iley 1990).

In summary, the highest resonance stabilization is observed between N and N and the highest rotational barrier for N-centered 3e-π bonds was predicted and found for hydrazine cation-radicals (Nelsen 1992). The barriers are, of course, lowered by delocalization onto substituents and by steric strain in the nearly planar, most stable form for species, which bear N-containing substituents.

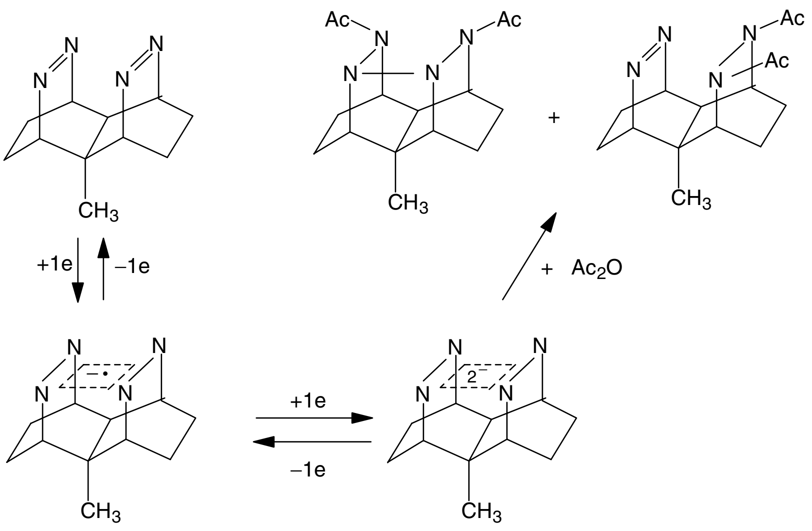
N-acetylmethionine amide [$CH_3SCH_2CH_2CH(NHCOCH_3)CONH_2$] gives the cation-radical with the 3e bond. The structure of the cation-radical depends on the pH. In acid solutions, the S∴S acyclic dimer is formed. In basic solutions, the S∴N five-membered cycle is produced between the atoms S on one hand and N belonging to the amide function on the other. This conclusion stems from recent studies using X- and Q-band time-resolving ESR spectroscopy (Yashiro et al. 2005). These authors observed no evidence for the S∴O bond formation leading to the six-membered cyclic cation-radical proposed by Schoeneich et al. (2000, 2003). It needs to be noted that the redox chemistry of methionine within proteins is currently a topic of great interest: One-electron oxidation of a methionine part in β-amyloid peptide has been associated with the neurotoxicity of that sequence. This peptide is the major constituent of senile plaques in Alzheimer's disease (Butterfield and Boyd-Kimball 2005).

Cation-radicals containing three electrons in the field of four atoms or anion-radicals with five electrons retained by four atoms represent a special group of multicentered ion-radicals. Thus, nonclassical, cyclically delocalized 3e/4C cation-radicals and 2e/4C (dication)-radicals of substituted cyclobutadienes are known (Allen and Tidwell 2001). The 3e/4N cation-radical and the 5e/4N anion-radical have also been discovered (Exner et al. 1998, 1999, 2000). The reactions in Scheme 3.31 illustrate structures of the 5e/4N anion-radical as well as the corresponding dianion and acetylated products of the latter.

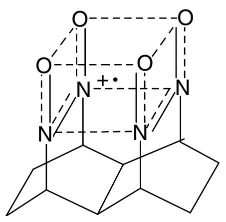
In the case of tetra(*N*-oxide) of the initial bis(diazene), one-electron oxidation in Scheme 3.32 leads to the formation of a novel, O-stabilized, 3e/4N cation-radical with 3-D delocalization of the unpaired electron (Exner et al. 1999).

3.2.4 Spin–Charge Separation (Distonic Stabilization of Ion-Radicals)

Localization of an unpaired electron in the framework of a definite molecular fragment can sometimes lead to the formation of ion-radicals with spatially separated charge and radical sites. They can be considered free radicals with an appended, remote charge. These species form a particular class of distonic ion-radicals. "Distonic" is from the Greek word *diestos* and the Latin word *distans*, both meaning "separate." Yates et al. (1984) introduced this term for ions that formally arise by the removal of an electron from a zwitterion or a biradical.



SCHEME 3.31

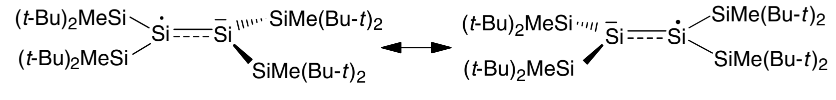


SCHEME 3.32

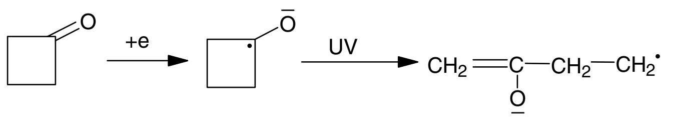
For instance, oxidation of most neutral closed-shell aromatic hydrocarbons generates cation-radicals that possess nearly coincident spin and positive-charge distribution. This distribution is approximated by the spatial density of the SOMO. However, cation-radicals derived from certain neutral organic biradicals can possess a more novel electronic structure, namely, ones in which spin and charge distributions are really noncoincident. In principle, this is possible because a biradical contains its two frontier electrons in a set of two degenerates or nearly degenerate molecular orbitals. Electron loss from a biradical can thus give a cation-radical whose spin distribution is a function of one orbital space and charge distribution is a function of another orbital space. If these two orbitals differ spatially, then the resultant cation-radical will be distonic (Radom et al. 1986). Such cation-radicals will possess different spin and charge sites, even within a fully conjugated π system.

Radom and coworkers used this term for systems containing a charge and an electron in two vicinal (side-by-side) positions (see, e.g., Gauld and Radom 1997). Nevertheless, the whole idea of the "distonic" ion-radicals as used by most of its practitioners is that the electron and the charge are separated by at least two heavy atoms between the charge and the radical sites. Such systems are also known (Kenttaemaa 1994, Gronert 2001). In this section, we will treat "truly distonic" systems, that is, systems in which there are sp^3-hybridized atoms between the radical and charge centers (or these centers do not overlap significantly). Such a definition is relevant to the principle of the detained electron and can help to distinguish ion-radicals with really separated charges and radical sites.

The denoted approach seems to be substantiated because the spin and charge locations can be changed in the distonic ion-radicals that are present side by side. For instance, tetrakis[di (*tert*-butyl)methylsilyl] derivatives of distannene (Fukawa et al. 2004) and disilene (Sekiguchi et al. 2004) give rise to stable alkali salts of anion-radicals in THF on reduction with potassium mirror in the presence of [2.2.2] cryptand or with *tert*-butyl lithium, respectively. The salts were obtained in 60–70% yields as red crystals. According to x-ray crystallography, there are no interactions between the anion-radicals and alkali cations. One tin/silicon atom of the distannene/disilene fragment and its *tert*-Bu_2MeSi substituents are located in the same plane, whereas the other tin/silicon with its



SCHEME 3.33



SCHEME 3.34

tert-Bu_2MeSi substituents has pyramidal geometry. These structural features of the anion-radical in the crystalline state testify for the separation of a spin and charge within the Sn—Sn or Si—Si bond: One of these atoms bears the negative charge, and the other acquires an unpaired electron. We have a typical side-by-side distonic anion-radical. However, rapid exchange takes place between atoms of Sn—Sn or Si—Si bond as it follows from the corresponding ESR spectra in 2-MeTHF. The exchange decelerates with the temperature drop. Scheme 3.33 illustrates this ambiguity of the side-by-side distonic ion-radicals.

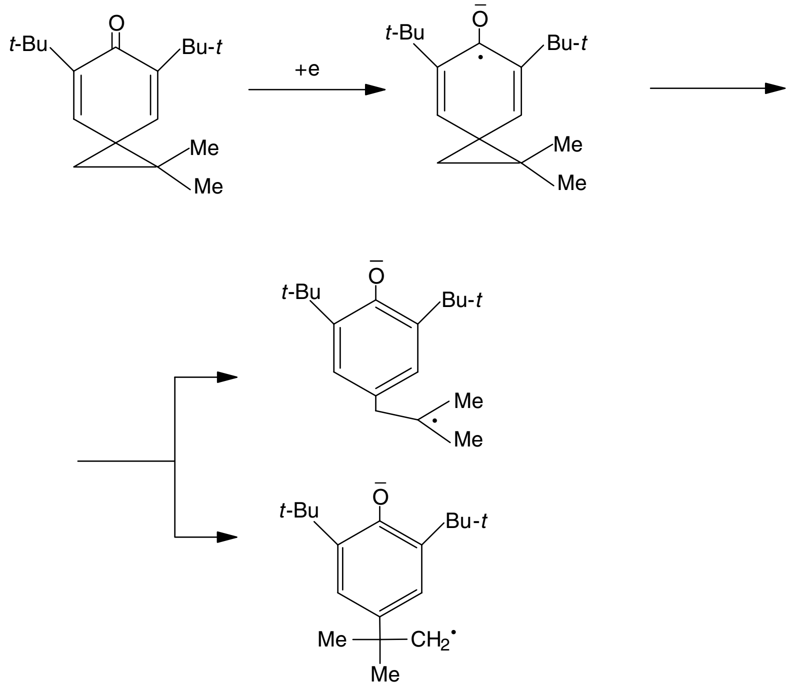
To complete the picture, works on anion-radicals of silicon and tin analogs of alkynes is cited. In the case of the related anion-radical from disilyne bearing two bulky substituents {—Si (2-Pr)[$CH(SiMe_3)_2]_2$} at both the sides of Si≡Si bond, the mentioned charge–electron separation is not observed. The anion-radical was prepared by reduction of the parent disilyne with potassium graphite in THF. The yield of the dark brown crystals was 63%. ESR, x-ray, and UB3LYP calculations show that the even delocalization of the unpaired electron within the $\{Si{\cong}Si\}^{-\bullet}$ bond is an intrinsic property of this anion-radical and is not dependent on the rate of electron exchange between the vicinal silicon atoms or pairing with the potassium cation (Kinjo et al. 2007). Takagi and Nagase (2007) calculated the energies of RSn≡SnR neutral molecule and its anion-radical based on the high-level (hybrid) density functional theory. According to the calculations, the more stable states are RSn≡SnR for the neutral molecule and $[RSn^{(\bullet\bullet)}\text{—}Sn^{(\bullet\bullet)}R]^{-\bullet}$ for the anion-radical. Transformation of the neutral molecule into the anion-radical brings about an Sn—Sn bond lengthening; this theoretical result is in line with the x-ray structural study of $\{[RGeGeR]^{-\bullet}\ [K(THF)_6]^{+\bullet}\}$ salt (Pu et al. 2003). The principles of distonic stabilization outlined here must be supplemented by considering distonic anion and cation-radicals separately.

3.2.4.1 Distonic Stabilization of Anion-Radicals

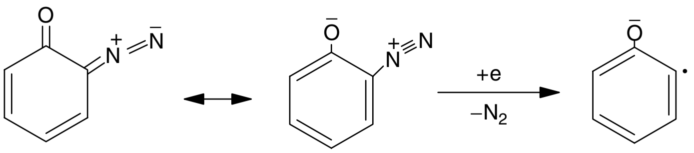
According to ESR spectra, cyclobutanone and tetramethylene sulfone undergo dissociative electron capture process (Scheme 3.34 for cyclobutanone) in argon matrices and yield distonic anion-radicals (Kasai 1991, Koeppe and Kasai 1994).

One-electron reduction of 1,1-dimethyl-5,7-di(*tert*-butyl)spiro[2,5]octa-4,7-diene-6-one leads to formation of anion-radical that undergoes ring opening (see Scheme 3.35). Relief of cyclopropane ring strain and the generation of an aromatic ring provide the thermodynamic driving force for this ring opening. Additionally, the spiro compound under consideration is a highly conjugated substrate, and the charge gained in producing the anion-radical is accommodated over an expanded contour. This results in little reorganization energy to reach the transition state. Two anion-radicals are eventually formed. In both the particles, the charged and radical centers are not in direct polar conjugation (Tanko et al. 1994, Tanko and Philips 1999, Stevenson et al. 2002).

Sometimes, distonic anion-radicals can be recognized among aromatic derivatives in which a radical center is strongly localized according to the structural peculiarities of the precursor molecule. In the sodium reduction of *o*-diazobenzophenone (Scheme 3.36), the formation of the radical center



SCHEME 3.35



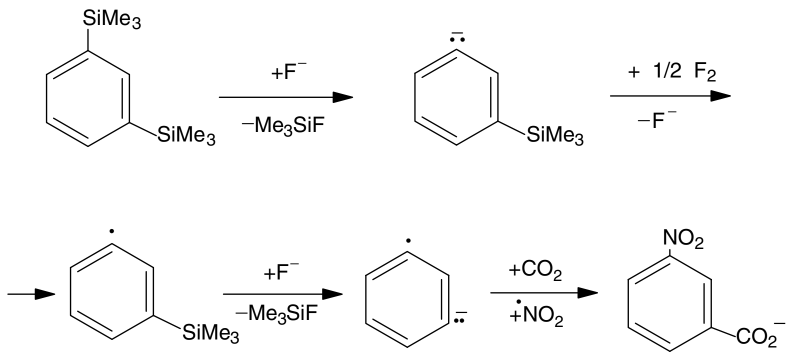
SCHEME 3.36

is a result of nitrogen elimination. At the same time, the carbonyl group transforms into an aprotic equivalent of the hydroxyl group. Analysis of the ESR spectrum of an anion-radical (isolated in an argon matrix) confirms its distonic nature (Hacker and Kasai 1993).

Calculations (Hacker and Kasai 1993) in the framework of extended Hueckel theory found the LUMO of *o*-diazobenzoquinone to be mainly (up to 60%) localized at the N—N sector. The electronegativity of the *o*-carbonyl oxygen enhances the acceptor properties of the diazo group. Charge-spin separation is an understandable consequence of the situation.

Scheme 3.37 describes gas-phase generation of *m*-benzyne anion (the distonic anion-biradical) from *m*-bis(trimethylsilyl) benzene (Wenthold et al. 1994, 1996; Wenthold and Squires 1998). The same anion-biradical is formed from isophthalic acid under the same conditions (Reed et al. 2000). Particularly, the reaction of *m*-bis(trimethylsilyl) benzene with fluoride ion, followed by treatment of the formed trimethylsilyl phenyl anion with fluorine in helium, produces the anion-biradical mentioned. The latter is transformed into the corresponding nitro benzoate anion through the addition of CO_2 and NO_2 (Scheme 3.37).

Interestingly, the stabilizing reagents (CO_2 and $^{\bullet}NO_2$) cannot be added in reverse order ($^{\bullet}NO_2$ first and CO_2 second) because the anionic site undergoes an electron-transfer reaction with $^{\bullet}NO_2$ faster than the radical site can add $^{\bullet}NO_2$. Conversion of the phenyl anion into the carboxylate eliminates the electron transfer pathway because the carboxylate has a higher electron-binding energy. This behavior again points to the dual reactivity of the distonic species.



SCHEME 3.37

Theoretical studies on the *m*-benzyne anion led to the inference that it holds a pair of weakly interacting orbitals. One orbital contains the odd spin density, whereas another contains two electrons that are responsible for the negative charge of this species (Nash and Squires 1996).

Also to be mentioned are the reactions of oxygen atom radical anions with organic substrates. These reactions were reviewed by Gronert (2001). For the reactivity of the atomic oxygen anion-radical, see Section 1.7.2. The atomic oxygen anion-radical reacts with benzene, tetramethylene ethane, or cyclopentadienylidene trimethylenemethane. The reactions consist in abstraction of H_2^+ with the formation of H_2O and the corresponding distonic anion-radicals as products.

3.2.4.2 Distonic Stabilization of Cation-Radicals

According to mass spectrometric studies by Bigler and Hesse (1995), α,ω-diaminoalkane cation-radicals undergo intramolecular hydrogen atom rearrangements leading to the formation of distonic cation-radicals:

$$H_2N(CH_2)_nNH_2 + e \rightarrow 2e + [H_2N(CH_2)_nNH_2]^{+\bullet}$$

$$[H_2N(CH_2)_nNH_2]^{+\bullet} \rightarrow H_3N^+(CH_2)_nNH^\bullet$$

The example of glycine is much more descriptive. The spin and charge separation has been found at the C- and the N terminus, respectively (Rodriguez-Santiago et al. 2000).

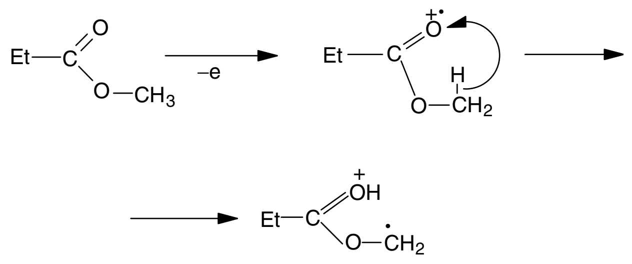
$$[H_2N]^{+\bullet}\text{–}CH_2\text{–}COOH \leftrightarrow [H_3N]^+CH_2COO^\bullet$$

The activation energy for this separation is 38 kJ mol^{-1} in the ground state, with no barrier in the first excited state (Nielsen et al. 2000). The driving force is the high proton affinity of the amino group. This leads to the formation of such stabilized distonic cation-radicals.

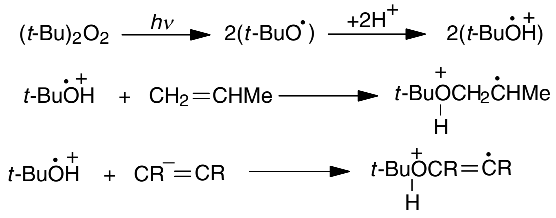
A similar explanation leads to the understanding of a separate existence of the conventional and distonic forms of the benzonitrile cation-radical, cf. $(H_5C_6C{\equiv}N)^{+\bullet}$ and $^\bullet H_4C_6C{\equiv}NH^+$ (Flammang et al. 2001). Although the distonic cation-radicals are less stable than the classical ones by ca. 45–50 kJ · mol^{-1}, they are protected against isomerization by a relatively high energetic barrier.

The example of the ethyl acetate cation-radical is also noteworthy (see Scheme 3.38). According to an ESR study (Rhodes 1988), on one-electron oxidation, ethyl acetate gives the onium (distonic) cation-radical and not the carbonyl (conventional).

The onium form of the ethyl acetate cation-radical is more stable by 50 kJ mol^{-1} than the corresponding carbonyl form (Rhodes 1988). The $CH_2^\bullet$ fragment is stabilized by the three-electron bonding with the neighboring oxygen in the following manner: –O∴CH$_2$. Oxidation of the carbonyl



SCHEME 3.38



SCHEME 3.39

group is very difficult, whereas oxidation of the hydroxyalkyl moiety is very easy. Meanwhile, the carbonyl oxygen atom can preserve its electron surrounding if converted into the onium state. In this case, however, an unpaired electron is localized on the methylene carbon atom and separated from the onium one with other heavy atoms. Therefore, the total stability of the distonic cation-radical becomes higher than that of the conventional one. All of the features mentioned also relate to the methyl benzoate cation-radical (see Scheme 3.38 and change Et with Ph). Mass spectrometric experiments and B3LYP calculations confirm this (Dechamps et al. 2006).

Distonic cation-radicals with onium ethereal oxygens are also known. For instance, addition of *tert*-butoxy radicals to ethylenic compounds was described by Bloodworth et al. (1988; Scheme 3.39). The butoxy radicals are added in their protonated forms (CF_3COOH is the proton source).

Studies on distonic ion-radicals have predominantly been performed during the past two decades with emphasis on theoretical approaches. A lot of experiments were carried out to prove their existence and observe their behavior (see reviews by Hammerum [1988] and Kenttaemaa [1994] and, an experimental work, for example, by Polce and Wesdemiotis [1996]). In the next stage, syntheses of distonic ion-radical organic salts that are stable under common conditions will probably be developed. These salts would be used to create magnetic, conductive, and other materials of practical use. In a chemical sense, the special strength of distonic organic ion-radicals is that they can, in principle, enter reactions of the ionic type at the charged center and reactions of the radical type at the radical center. For instance, the distonic anion-radical of cyclopentadienylidene trimethylenemethane reacts under mass spectrometer gaseous-phase conditions with carbon disulfide by sulfur abstraction and with nitric oxide by NO-radical addition. The first reaction characterizes the distonic anion-radical mentioned as a nucleophile bearing a negatively charged moiety. The second reaction describes the same anion-radical as a species having a group with radical unsaturation (Zhao et al. 1996).

For another example of the strong duality in the chemical behavior of distonic cation-radicals, see Moraes and Eberlin (1998). In the gaseous phase, *m*- and *p*-dehydrobenzoyl cation-radicals ($^{\bullet}C_6H_4C^+{=}O$) react selectively either as free radicals or as acylium ions, depending on the choice of the reacting partner. Transacetalization with 2-methyl-1,3-dioxolane, ketalization with 2-methoxyethanol and epoxide ring expansion with epichlorohydrin demonstrate their acylium reactivity.

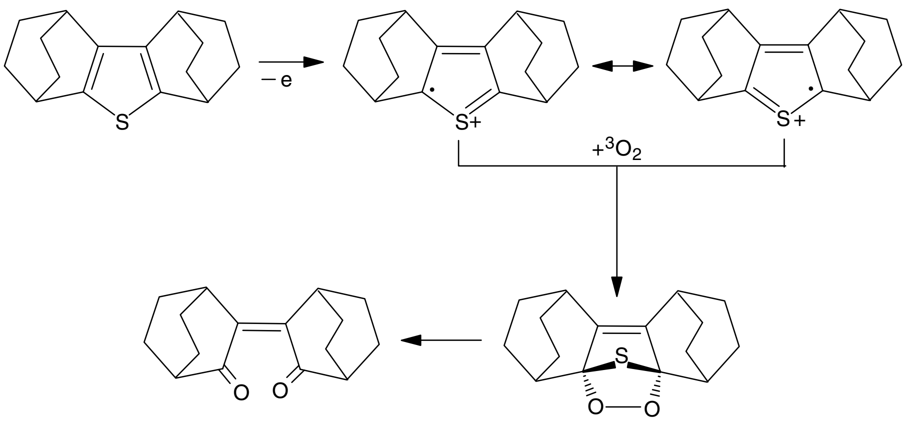
The free-radical reactivity stems from abstraction of (•SMe) from MeSSMe. In the reactions with gaseous mixtures of epichlorohydrin and dimethyldisulfide, the *m*- and *p*-dehydrobenzoyl cation-radicals react selectively at either site to form the two monoderivatized ions. Further reaction either at the remaining radical or at the acylium charge site leads to a single biderivatized ion as the final product. Tomazela et al. (2006) scrutinized the electronic structure of $^{\bullet}C_6H_4C^+{=}O$ by performing *ab initio* MO calculations. As turned out, these cation-radicals cannot be suitably classified as distonic species with spatially separated radical and spin sites. Their radical nonsaturations are indeed σ localized, but their positive charges are delocalized within the π molecular systems. Many examples of similar distoniclike species can be classified as distonoid ion-radicals (Tomazela et al. 2006). Ion-radicals are, consequently, divided into three subclasses: conventional, distonic, and distonoid.

It would be very important to find reactions of the distonic or distonoid ion-radicals in the liquid phase. Successes in studies of such dual reactivity in liquid phase may seriously widen possibilities of organic synthesis. There are only few works of this kind and they are of importance to be cited.

In simple olefins of the stilbene type, cis → trans isomerization in the cation-radical state is known to proceed readily because the exocyclic double bond is weakened. In the case of the 1,2-di(aryloxy)cylobutane cation-radical, cis → trans isomerization also takes place (see Evans et al. 1975), but the reaction inevitably should include the open form of the distonic type, $ArOCH^{\bullet}\,CH_2{-}CH_2CH^+OAr$. Free rotation in this distonic cation-radical around $CH_2{-}CH_2$ bond permits ensuing ring closure with the formation of the more stable *trans* isomer.

Methyl tricyclo[4.1.0.0^{2,7}]heptane-1-carboxylate gives a cation-radical in which the spin density is almost completely localized on C-1 while the positive charge is on C-7. The revealed structural feature of the intermediate cation-radical fairly explains the regioselectivity of *N*,*N*-dichlorobenzenesulfonamide addition to the molecular precursor of this cation-radical. In the reaction mentioned, the nucleophilic nitrogen atom of the reactant adds to electrophilic C-7, and the chlorine radical attacks C-1 whose spin population is maximal (Zverev and Vasin 1998, 2000).

Wakamiya et al. (2002) prepared and isolated the hexafluoroantimonate salt of a thiophene cation-radical in which the cation-radical part was stabilized by annelation as shown in Scheme 3.40. According to ESR spectra and MO calculations, the 2,5-carbon atoms of the thiophene ring share spin density, whereas the positive charge is mainly localized on the sulfur atom. In solutions, this cation-radical reacts with the triplet (i.e., biradical) oxygen, adding it cojointly to positions 2 and 5 of the thiophene ring. The final product of this liquid-phase reaction is 1,4-diketene (see Scheme 3.40). This strong radical reactivity supports the distoniclike structure of the key



SCHEME 3.40

species, namely, the cation-radical. It should be especially emphasized that the cation-radical is characterized by the localization of the positive charge on sulfur and by sharing the spin density between α and α′ positions of the heterocycle. Therefore, the species can be better classified as a distonoid ion.

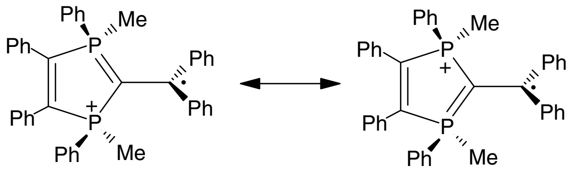
A similar situation is observed in the case of the cation-radical derived from dimethylhexaphenyl diphosphafulvenium dication as a result of reduction of the latter by the sodium salt of the naphthalene anion-radical (Biaso et al. 2006). According to ESR, x-ray experimental data, and results of DFT calculations, the diphosphafulvenium cation-radical detains the excess electron density within the exocyclic double bond (see Scheme 3.41). Stabilization is gained by conjugation with the two pentavalent phosphorus atoms. Biaso et al. (2006) rationalize the electronic structure through two valence-isomeric fluidic forms of the distonic type.

3.2.5 Ion-Pair Formation

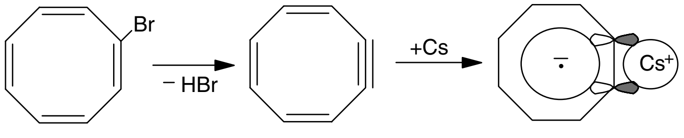
Organic ion-radicals exist together with counterions and often form ion pairs. Since the pioneering works of Grunwald (1954), Winstein et al. (1954), and Fuoss and Sadek (1954), the terms *contact*, *tight*, or *intimate ion pair* and *solvent-separated* or *loose ion pair* have become well known in the chemical world. Afterward, Marcus (1985) and Boche (1992) introduced other colloquial expressions, the *solvent-shared ion pair* and the *penetrated ion pair.* There are also several initial publications concerning the so-called alkali zwitterion-radicals. For example, dehydrohalogenation of bromocyclooctatetraene followed by alkali metal reduction generates an anion-radical in which an excess electron is delocalized within an eight-membered ring, and an alkali cation interacts with the "double" bond that is not involved in the ring delocalization (see Scheme 3.42). This "double" bond is derived from the triple bond, which formerly existed in the dehalogenation product: One π-electron pair takes part in the formation of ring π contour, but another π-electron pair remains isolated. An alkali cation of the appropriate size (K^+ and Cs^+ but not Na^+) is installed in such a way that a very unusual overlap is achieved between the *p* orbitals of the "double" bond and the empty 4*s* orbital of the alkali cation (Peters et al. 2003, Kiesewetter et al. 2005).

Scheme 3.42 represents a novel and intriguing case of ion pairing. It would be essential to explore generality of this type of ion pairing and elucidate its importance in organic chemistry. Meanwhile, the literature on conventional types of ion pairing contains many records confirming their significant role in ion-radical transformations.

In solvent-separated ion pairs, the primary solvation shells of the cation and the anion actually remain intact. In solvent-shared ion pairs, a single solvent molecule exists in the space between the



SCHEME 3.41



SCHEME 3.42

counterions. In a contact ion pair, there is no solvent molecule between the counterions; they are in direct contact and are surrounded by a common solvation shell. In a penetrated ion pair, an empty space between the edge groups in one ion of a salt is occupied to a certain degree by another (counter) ion. The two latter types of ion pair may have quite a different electronic distribution than the corresponding "naked" ions. In connection with the examples provided here, it is pertinent to look a little more closely at the relationship between ion pairing and complexation. There is an authoritative point of view (Marcus and Hefter 2006) that the difference between these two phenomena "is largely semantic." However, fastening between spin-bearing fragments of anion-radicals and alkali metal cations in our cases is so strong that it borders covalent binding and can be considered as real ionic complexation; the corresponding examples are presented.

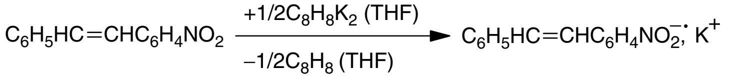
3.2.5.1 Detention of Unpaired Electron in a Framework of One Specific Molecular Fragment

A single-electron transfer from cyclooctatetraene dipotassium ($C_8H_8K_2$) to 2- and 4-nitrostilbenes in THF leads to the formation of paramagnetic potassium salts of the anion-radicals. In this solvent, the salts exist as coordination complexes (Scheme 3.43).

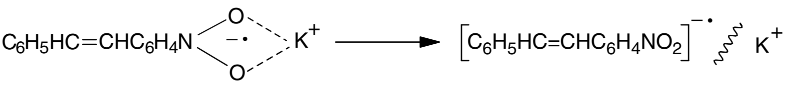
The complexes can be destroyed by the addition of 18-crown-6-ether or HMPA to the THF solution (Scheme 3.44). Such dissociation has been proven by ESR spectra (Todres 1992).

On one-electron reduction followed by one-electron oxidation, cis isomers of 2- and 4-nitrostilbenes turn into the neutral nitrostilbene molecules, but in the trans forms. On oxidation of the "naked" anion-radicals, the neutral trans forms are the only products (cis → trans conversion degrees were 100%). In the case of the coordination complexes, the trans isomers are formed only up to 40% (Todres 1992). Scheme 3.45 describes these transformations.

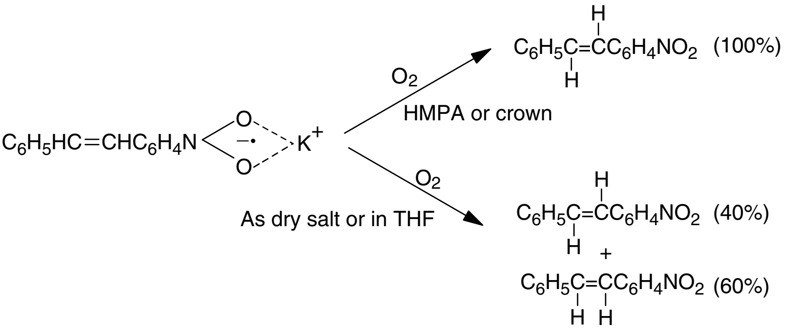
Thus, one-electron transfer causes cis → trans isomerization. It is quite effective with free migration of an unpaired electron over the molecular framework. It is less effective when the unpaired electron is confined within the limits of a coordination complex. Such fixation of the unpaired electron hinders the rotation around the C=C bond. In a similar manner, a ball tied to a



SCHEME 3.43



SCHEME 3.44



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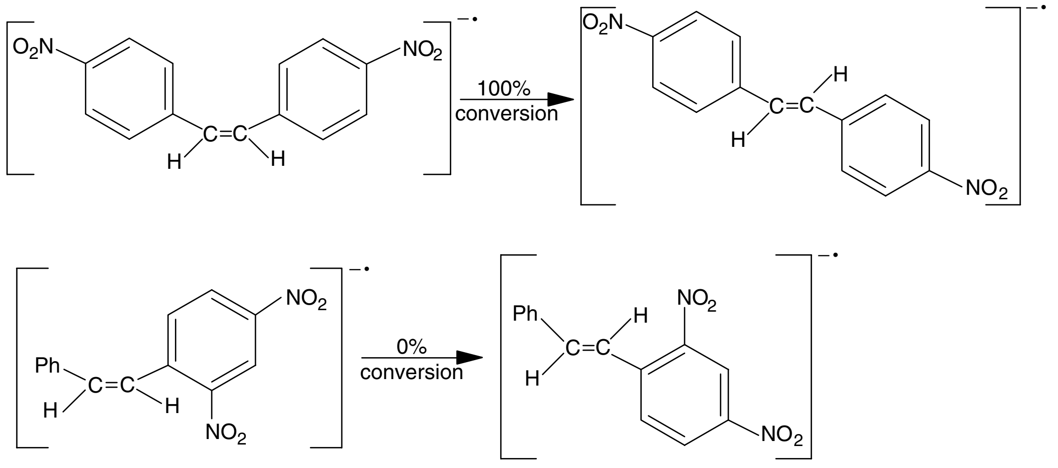


SCHEME 3.46

finger with a rubber band flies on being struck until the rubber band stretches out to its utmost, and then the ball abruptly returns to the finger, to the ball's initial point of movement.

The isomerization is more effective when the (nitroanion-radical + alkali counterion) ion pair does not exist. The following needs to be noted: It is assumed that intimate ion pairs possess larger electron affinity and are characterized by larger contribution to the free energy of electron transfer than free ions (Grigoriev et al. 2001).

Now let us compare 4,4′- and 2,4-dinitrostilbenes with respect to their relative capabilities to rotate around the C=C bond on electron transfer. The difference between them is shown in Scheme 3.46 (Todres et al. 1980).

It is clear that an unpaired electron oscillates between two nitro groups in the 4,4′-dinitro derivative and is retained in the dinitrophenyl ring in the 2,4-dinitro compound. The potassium salt of the 2,4-dinitrostilbene anion-radical does not change the initial cis geometry, even in the presence of crown ether. It is known, however, that *trans*-2,4-dinitrostilbene is more stable than the cis isomer (Pfeifer et al. 1915), therefore once again, cis-to-trans isomerization is highly correlated with the spin population of the C=C bond. The quantum-chemical considerations unambiguously established such correlation (Dyusengaliev et al. 1981).

The potassium salt of the 2,2′-dipyridyl acetylene anion-radical represents another important example. In this case, the spin and charge are localized in the framework of N–C–C≡C–C–N fragment. The atomic charge on each nitrogen atom is −0.447, that is, close to unity in total. The energy of this ion pair is minimal when the potassium counterion is located midway between the two rather close nitrogen lone pairs. Such a structure is consistent with the fact that the ESR spectrum of this species is almost insensitive to temperature. It means that the counterion does not hop between two remote sites of the anion-radical (Choua et al. 1999).

3.2.5.2 Formation of Closed Contour for Unpaired Electron Delocalization

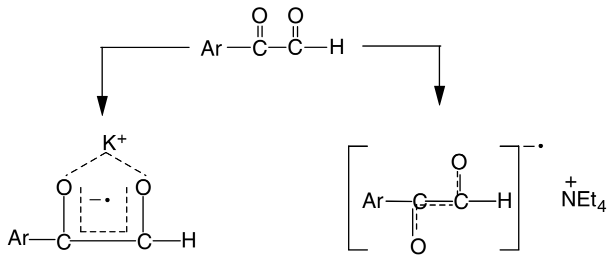
This phenomenon can efficiently restrain an unfavorable configuration. It is well known that in 1,2-semidione anion-radicals, the *trans* isomer has a higher stability owing to the minimization of dipole–dipole repulsions. Nevertheless, the presence of a counterion may change the isomer distribution by favoring the cis structure, drawing together the two negatively charged oxygen atoms. As calculations (Calle et al. 1992) show, the preferential approach of an alkaline cation to a 1,2-semidione is indeed in the middle of the two oxygen atoms. A cation-semidione chelate (or a penetrated ion pair) is formed, the equilibrium distance being approximately 0.23 nm. This

conformation is 120 kJ · mol^{-1} more stable than the corresponding trans conformation. Divalent cations must be closer to the semidiones than the monovalent ones (Be^{2+} and Mg^{2+} were calculated to be closer than Li^+ and Na^+, respectively). Both Be^{2+} and Mg^{2+} cations stabilize the cis isomer better than Li^+ and Na^+ cations (Calle et al. 1992). This is due to a stronger electrostatic interaction associated with the charge.

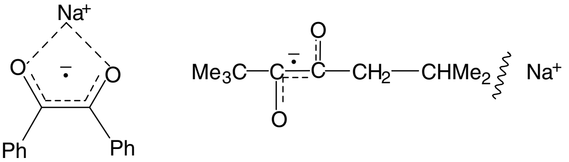
The one-electron reduction of 3,4,5-trimethoxyphenyl glyoxal with potassium *tert*-butoxide in DMSO gives rise mainly to the *cis*-semidione, whereas on electrolysis in dimethylformamide, in the presence of tetraethylammonium perchlorate as the carrier electrolyte, the main product is the trans isomer (Sundaresan and Wallwork 1972; Scheme 3.47).

The ESR spectrum of the sodium salt of dibenzoyl ketyl in THF shows splitting due to Na^+, whereas in the ESR spectrum of the sodium salt of the ketyl of 2,2,6,6-tetramethylhexane-3,4-dione in THF, there is no splitting whatever due to Na^+ (Luckhurst and Orgel 1963). Although dibenzoyl ketyl can give rise to the contact (or penetrate) ion pair, the formation of such a type of species from the 3,4-dione is difficult, owing to steric hindrance. This semidione exists in the form of a free ion (or an ion pair separated by solvent molecules); compare the two structures given in Scheme 3.48.

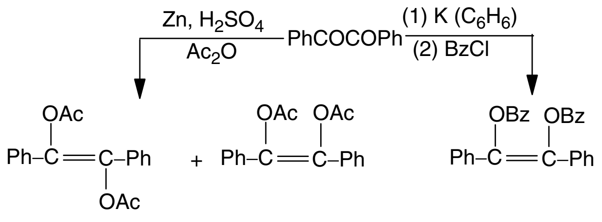
If the dibenzoyl ketyl ion is not included in the ion-pair complex with the alkali cation, it exists in the trans form. The potassium salt exists in the cis form, in which both charged oxygen atoms are in the vicinity of the metal cation (Bauld 1965). On benzoylation, the cis ion-radical pair gives rise mainly to *cis*-dibenzoyl stilbene. Meanwhile, the reduction of dibenzoyl under conditions, which do not stabilize the contact ion pair, is not stereospecific (Bauld 1965, Thiele 1899). Scheme 3.49 compares the results of these two different reactions of the same substrate.



SCHEME 3.47



SCHEME 3.48



SCHEME 3.49

The relation between the spin density distribution in the products of electron transfer to organic molecules and the behavior of these products in further reactions is considered here. This relation is important, but has not been investigated much so far. It would be especially useful to know the reason for the particular sequence of chemical changes in the groups present simultaneously in the molecule. Let us compare the results of the one-electron and multielectron reductions of 4,4′-dinitro dibenzoyl. The one-electron reduction leads to a paramagnetic species whose ESR spectra depend on temperature and concentration. As shown (Maruyama and Otsuki 1968), such electron transfer products can exist in the monomeric or dimeric form. The monomer is present at a high dilution. The dimer forms at an increased concentration or at a low temperature (see Scheme 3.50).

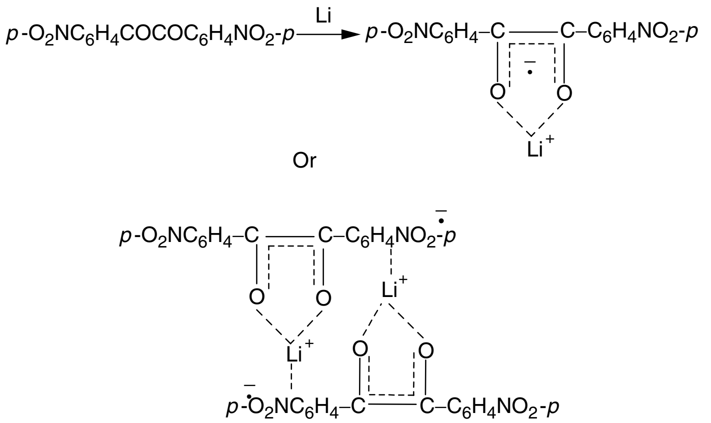
In the monomeric form, the unpaired electron is delocalized mainly over the dicarbonyl moiety, and in the dimeric form, over the nitro groups. Under the conditions favoring the dimer formation, 4,4′-dinitrobenzophenone gives rise to anion-radicals in which the nitro- and not the carbonyl group carries the maximum electron density (Maruyama and Otsuki 1968). These results of the analysis of the ESR spectra are consistent with chemical data. For example, on reduction with tin in hydrochloric acid, 4,4′-dinitrobenzophenone forms 4,4′-diaminobenzophenone (only the nitro groups are reduced; Staedel 1883). Under the same conditions, 4,4′-dinitrodibenzoyl gives 4,4′-diaminodesoxybenzoin (both nitro and carbonyl groups are reduced; Golubeff 1873):

$$4\text{-}O_2N\text{–}C_6H_4\text{–}CO\text{–}C_6H_4\text{–}NO_2\text{-}4' \rightarrow 4\text{-}H_2N\text{–}C_6H_4\text{–}CO\text{–}C_6H_4\text{–}NH_2\text{-}4'$$

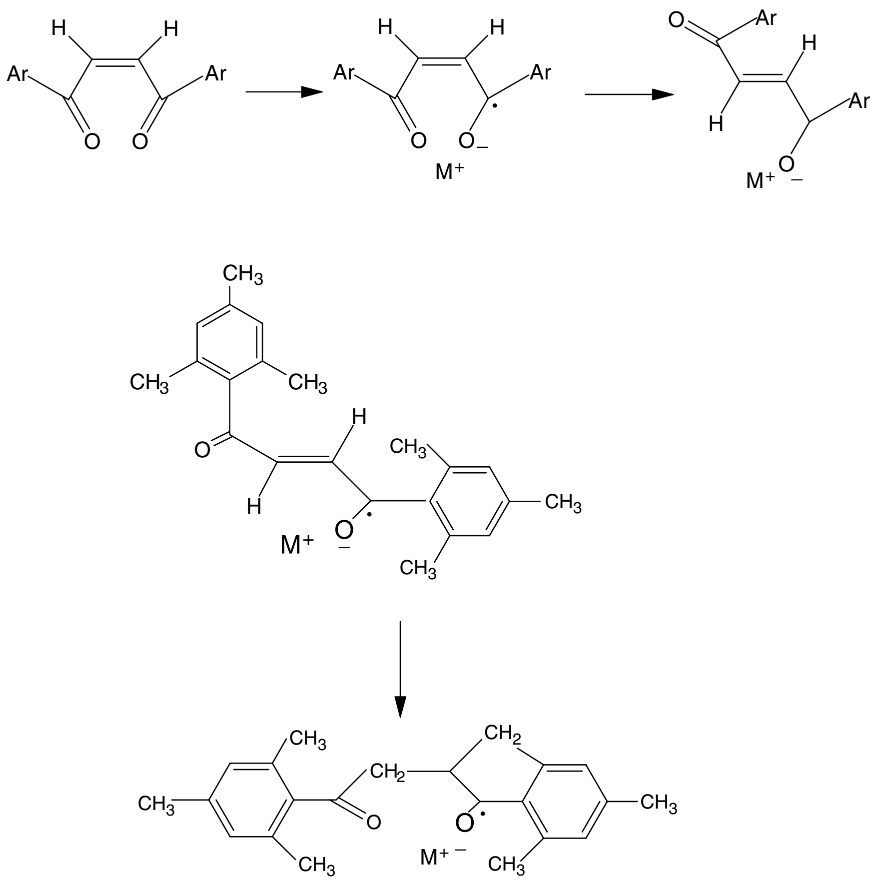
$$4\text{-}O_2N\text{–}C_6H_4\text{–}CO\text{–}CO\text{–}C_6H_4\text{–}NO_2\text{-}4' \rightarrow 4\text{-}H_2N\text{–}C_6H_4\text{–}CO\text{–}CH_2\text{–}C_6H_4\text{–}NH_2\text{-}4'$$

The metals Li, Na, K, Cs, and Hg-amalgam of Mg have been employed as reducing agents for trans and cis 1,4-diones (see the combined Scheme 3.51; Lazana et al. 1993). It was found that cis isomeric ion pairs are favored under conditions involving greater ion association, such as with small counterions, low solvating power of the solvent, and at high temperatures. Isomerization of the cis → trans type occurs at −80°C even for lithium ion pairs in DME. Contact (tight) ion pairs tend to transform into solvent-separated (loose) ion pairs with a temperature decrease. Except for the small $Li^+$and Mg^+ counterions associated with a 1,4-dione, the ion pairs with the trans configuration undergo cyclization, with the formation of a new five-member ring (bottom structure of Scheme 3.51).

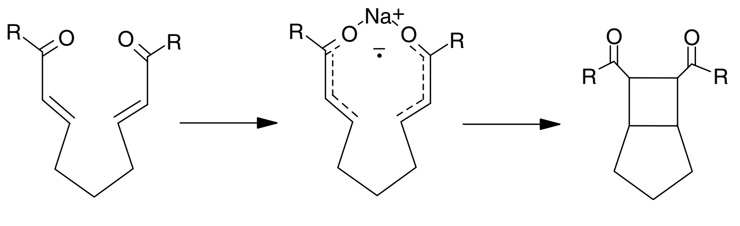
The formation of the bottom structure in Scheme 3.51 seems surprising. The related semidione from 1,4-dimesitylbutatetra-1,2,3,4-one (dimesityl tetraketone) forms ion pairs with Na^+, Cs^+, and Ba^{2+} but do not exhibit any chemical reactions (Bock et al. 1990).



SCHEME 3.50



SCHEME 3.51



SCHEME 3.52

The sodium cation chelation by the bis(enone) anion-radicals shown in Scheme 3.52 controls their further transformations although they proceed at the expense of other reaction centers (Yang et al. 2004). This kind of intramolecular cyclobutanation is characterized with the pronounced cis-stereoselectivity. However, this stereoselectivity disappears if the reaction proceeds in the presence of the tetrabutylammonium cation, when such a chelation is impossible.

In the case of alkali metals, ion pairing can be visualized as HFCs from paramagnetic nuclei of the metal cations associated with organic anion-radicals in ethereal solvents. In this respect, an alkali metal cation associated with the anion-radical of *o*-dimesitoylbenzene in DME or THF serves as a paradigm (Herold et al. 1965).

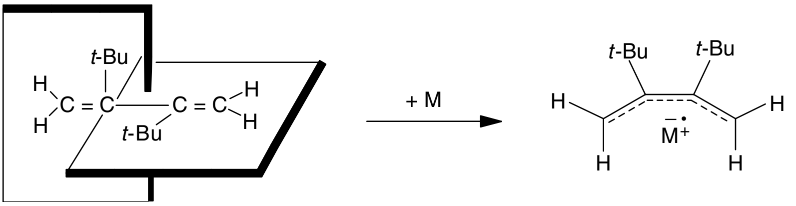
All of the examples considered in this section up to now, have carbonyl (chelating) groups. Alkali salts of anion-radical *without* chelating groups should also be considered, to complete the picture.

Melloni and coworkers considered a situation similar to the one applied to alkyl aryl ethers. They found that the position of the counterion (together with the relative orientation of the alkyl ethereal bond with respect to the benzene ring plane) is the main factor governing the regioselectivity of the anion-radical fragmentation in alkyl aryl ethers. The ethers can undergo both dealkylation and dealkoxylation. Dealkoxylation occurs when an alkali metal cation is coordinated with the oxygen atom of the ethereal bond. If such coordination is destroyed (e.g., in the presence of crown ethers), significant amounts of dealkylation product are obtained. In the same work, a free-energy calculation was performed for C—O bond fragmentation in alkyl aryl ether anion-radicals (Casado et al. 2000). This calculation shows that such an anion-radical system, when no external influences are present, has a significant thermodynamic driving force in favor of dealkylation. Consequently, the formation of a oxygen–metal ion pair allows overcoming of the thermodynamic restriction and directs the fragmentation to the cleavage of AlkO—C bond.

It seems that some strong association with the countercation should be favored by the compactness of the π system in the organic anion-radical. The two main factors can be seen as defining this association. First, the lower electron affinity of a small π system is expected to ease a partial retrotransfer of an unpaired electron to the countercation. Second, a higher degree of localization of the negative charge in such a π system should strengthen the association of the cation with the anion-radical. These assumptions suggest that the anion-radical of ethene, a two-center π system, would be the best candidacy for such a purpose. Not ethene, with an isolated π system, but 1,3-butadiene and its derivatives give observable anion-radicals (Levy and Myers 1964, 1966). Of course, the reaction of 1,3-butadiene and its derivatives with the alkali metal in an ethereal solvent fails to yield a persistent anion-radical because of rapid polymerization to rubberlike products. This process is, however, hindered by bulky alkyl substitution (Gerson et al. 1998). The ion pairs between the anion-radical of 2,3-di(*tert*-butyl)-1,3-butadiene and cations of potassium, rubidium, or cesium will be considered concerning Scheme 3.53.

Both theory and experiment point to an almost perpendicular orientation of the two butadiene $H_2C{=}C(t\text{-Bu})$ moieties (see Scheme 3.53). On passing from the neutral molecule to its anion-radical, this orthogonal orientation should flatten because the LUMO of 1,3-butadiene is bonding between C-2 and C-3. Therefore, C2-C3 bond should be considerably strengthened after the anion-radical formation. The anion-radical will acquire the *cisoidal* conformation. This conformation places two bulky *tert*-butyl substituents on "one side" of the molecule, so that the alkali metal counterion (M^+) can approach the anion-radical from the "other side." In this case, the cation will detain spin density in the localized part of the molecular skeleton. A direct transfer of the spin population from the SOMO of the anion-radical into the alkali cation has been proven (Gerson et al. 1998).

Low-lying vacant orbitals of alkali metal cations can, consequently, accept an unpaired electron density even if it is delocalized over an extended π system of carbon chains. The anion-radical of 1,4-diphenylbutadiene can exist in *s*-trans and in *s*-cis forms. The relative amounts of these geometrical isomers appear to depend highly on the counterion/solvent system. Li^+ and K^+ were studied as counterions; THF, 2-MeTHF, and DME were employed as solvents (Schenk et al. 1991). Interaction between the anion-radical and the cation contributes to a stabilization of



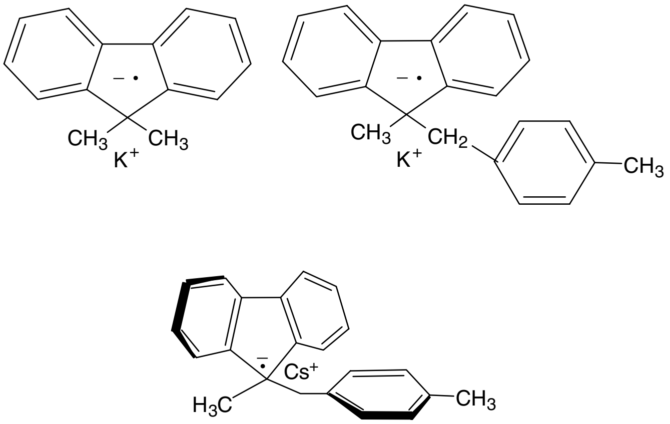
SCHEME 3.53

the *s*-cis arrangement "if the cation is close to the carbons C-1 and C-4." This stabilization is the most pronounced in an ion pair with a close interaction of the countercation and the π system and, indeed, the *s*-cis form of the anion-radical is only observed under those experimental conditions that favor tight ion pairing.

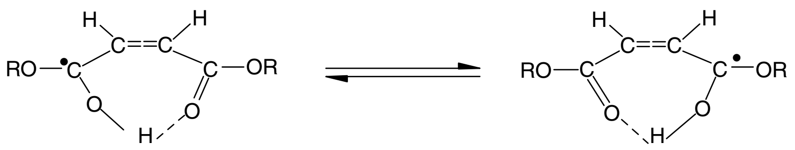
One case of π—*s*—π delocalization was demonstrated by Stevenson et al. (2006). The potassium anion-radical salt of 1-(9-methyl-9H-fluoren-9-yl)-4-methyl benzyl is characterized by the delocalization of an unpaired electron within the fluorenyl moiety only. Its ESR spectrum completely coincides with the spectrum of the potassium anion-radical salt of the 9,9-dimethyl fluorene anion-radical in THF. However, the cesium anion-radical salt of the fluorenyl methylbenzyl derivative produces the ESR spectrum corresponding to the placement of this cation between the fluorenyl and methylbenzyl moiety. The conditions of π—s—π delocalization appear: An unpaired electron spends its time within both fluorenyl and methylbenzyl fragments. The situation is explained in Scheme 3.54.

Stevenson et al. (2006) estimated the height of the cavity between the fluorenyl and methylbenzyl fragments in the anion-radical of Scheme 3.54 to be 0.35 nm. According to Marcus (1994) table, the ionic diameters are equal to 0.28 nm for K^+ and 0.34 nm for Cs^+. It is lucid that K^+ is too small to physically fill the gap between the two isolated π systems. On the contrary, Cs^+ is about perfect to bridge the gap over and complete an effective overlap of the unoccupied *s* orbital of the cation with the π orbitals of both the moieties of the anion-radical.

Of course, not only metal cations are able to gather a delocalization contour for an unpaired electron in ion-radicals. There is an extensive body of works studying the role of proton in meeting ring ends. Therefore, only the most prominent example will be considered here. It was shown that in pyridine, DMSO, and dimethylformamide, dialkyl fumarates or dialkyl maleates are reduced in a stepwise manner (Takahashi and Elving 1967, Nelsen 1967, Il'yasov et al. 1971a). Anion-radicals capable of undergoing one-electron oxidation are formed at the first stage. The half-wave potential for the reduction of maleate and fumarate differ, but the one-electron oxidation of the resulting anion-radicals is characterized by the same half-wave potential. This relation between the $E_{1/2}$ for the cathodic and anodic waves also holds at a very high alternating frequency, up to 500 Hz (Il'yasov et al. 1971a). Yeh and Bard (1977) obtained the same results. This implies that the anion-radicals from maleate and fumarate have similar energies. The ESR spectra of the products of the electrochemical reduction of dimethyl fumarate and maleate are identical at the potential of the limiting currents of the first waves (Il'yasov et al. 1971b). According to the authors, it is unlikely that the ESR spectra of the cis and the trans anion-radicals are completely identical. Thus, it is assumed that the ESR spectra of the cis and trans anion-radicals should differ, and the preceding observation



SCHEME 3.54



SCHEME 3.55

indicates a rapid and almost complete trans isomerization of the cis anion-radicals. At the same time, if the anion-radicals are obtained in a proton-donating medium, the cis and trans isomers give rise to different ESR (Anderson et al. 1971) and electronic (Hayon and Simic 1973) spectra. Under these conditions, maleates evidently give rise to unusually stable anion-radicals whose structure is fixed by the formation of a ring with the participation of a proton from the medium. Scheme 3.55 illustrates this phenomenon.

It needs to be noted that intra- or intermolecular hydrogen bonding is significantly enforced for the anion-radical states. Thus, the neutral tetrazine species demonstrate a relatively weak single hydrogen bond with *N*,*N*′-diethylthiourea. One-electron reduction of the tetrazines leads to the formation of two hydrogen bonds between the host and the guest within the seven-membered cycles (Jordan et al. 2007). The reduced tetrazines provide a significant negative charge on the nitrogen atoms in the tetrazine core. Naturally, a stronger interaction establishes with the partially positive-charged hydrogen atoms of the thiourea derivatives. This results in the enhancement of the hydrogen bonds in the overall host–guest complex.

Besides stereochemical effects, the formation of closed ion-paired contours can change the very reactivity of organic ion-radicals. Coordination of the potassium cation to two oxygen atoms in the anion-radical of *o*-dinitrobenzene leads to the stabilization of an unusual configuration in which the nitro groups are spread out in a single plane. In neutral *o*-dinitrobenzene, the coplanarity of the two nitro groups is ruled out by calculation (Ghirvu et al. 1971) and experiment (Calderbank et al. 1968, Myagi 1971). In the potassium derivative of *o*-dinitrobenzene, the coordination of the metal cation to both nitro groups leads to the formation of a condensed "ring" in which there is a possibility of an additional delocalization of the unpaired electron. Indeed, the ESR spectra in DME or THF show that the unpaired electron in this species is equally delocalized over the two nitro groups (the constants for the splitting by the nitrogen atoms $a_N^1 = a_N^2 = 0.32$ mT; Ward 1961). Meanwhile, in the potassium salt of the anion-radical of *m*-dinitrobenzene, the delocalization takes place essentially over only one of the two groups ($a_N^1 = 0.93$ mT, $a_N^2 = 0.02$ mT; Ward 1961, Gol'teuzen et al. 1972). This contrasts sharply with ESR spectroscopic data of the anion-radicals obtained by electrolysis in AN in the presence of tetra(*n*-propyl) ammonium perchlorate as the supporting electrolyte; $a_N^1 = a_N^2 = 0.32$ mT for the *o*-dinitrobenzene anion-radical and $a_N^1 = a_N^2 = 0.47$ mT for the *m*-dinitrobenzene anion-radical (Maki and Geske 1960). The difference can be understood if the nature of the counterion is taken into account. In the case of the potassium cation, the formation of a closely knit ion pair is possible. The K^+ ion can then provide its low-lying vacant *d* and *p* orbitals to be populated with the π electrons of the "condensed" anion-radical system.

When a tetraalkylammonium cation is used as a counterion in solvents of high polarity, such as AN or DMF, the alkyl groups of the cation hinder the mutual approach of species with different charges. Ion pairs with the potassium cation are stable. This follows from a comparison of the polarographic behavior of the three isomeric dinitrobenzenes in the same solvent (DMF) using tetraethylammonium or potassium perchlorate as the carrier electrolyte (Todres 1970). The half-wave potentials corresponding to the conversion of *p*- and *m*-dinitrobenzenes into anion-radicals are independent of whether tetraethylammonium or potassium counterions are employed. The anion-radical is formed from *o*-dinitrobenzene at a potential that is less negative by almost 100 mV when

tetraethylammonium perchlorate is replaced by potassium or sodium perchlorate. Under these conditions, changes in the composition and structure of the electrical double layer do not influence the reduction mechanism, which has been shown by a special study (Todres et al. 1972) to consist of the reversible transfer of one electron. Since the transfer of one electron to *o*-dinitrobenzene in the presence of potassium perchlorate as the carrier electrolyte proceeds at a less negative potential than in the presence of tetraethylammonium perchlorate, it is clear that the potassium salt indeed has the minimal energy.

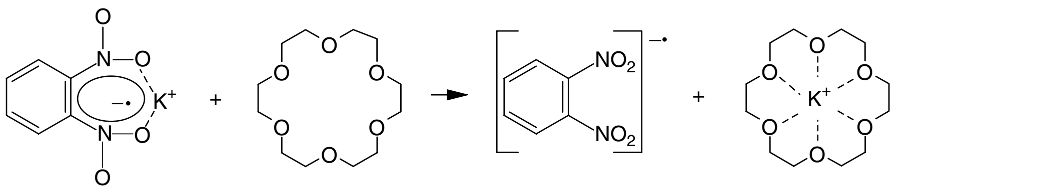
It was ion pairing between the potassium cation and the *o*-dinitrobenzene anion-radical that gave the first successful example of anion-radical azo coupling. Perhaps, azo coupling is the most characteristic and practically used reaction in aromatic range. An indispensable requirement for this reaction is the presence of the amino or hydroxyl group in an aromatic substrate. Azo coupling reactions with aromatic compounds containing only the nitro groups were deemed impossible. As was established (Todres et al. 1988a), the potassium salt of the anion-radical of *o*-dinitrobenzene reacts with benzene diazo cations in THF undergoing azo coupling at the para position (see Section 1.2.1). The azo coupling mentioned earlier is accompanied by the conversion of one of the nitro groups into the hydroxyl group. Hence, the radical product is stabilized by eliminating the nitrogen monoxide radical. All the radicals are prone to stabilize by expelling a small radical particle. This is the case, too. And nitrogen monoxide was established as a gas-phase product of the reaction (Todres et al. 1988a). As a result of quantum-chemical calculations on the *o*-dinitrobenzene anion-radical (Todres 1990), the attack of cation-type electrophiles is predicted to take place at the two para positions of the benzene ring. Ortho substitutions seem impossible. The experiments have confirmed this theoretical prediction.

An azo coupling could be prevented by changing THF as a solvent to DMSO or by adding 18-crown-6-ether to the THF-reaction mixture. The splitting of the coordination complex is illustrated in Scheme 3.56.

When the coordination complex is destroyed, no azo coupling takes place. In this case, only electron transfer products are formed, namely, *o*-dinitrobenzene, a benzene derivative RC_6H_5 from $RC_6H_4N_2BF_4$, gaseous nitrogen, and KBF_4.

From this point of view, the studies on the interaction of benzene diazo cations with the potassium salt of the *p*-dinitrobenzene anion-radical should be mentioned (Todres et al. 1988b). The potassium cation in such an anion-radical salt is known to be located near one of the nitro groups. This lone nitro group bears the main part of the spin density (Ling and Gendell 1967). In a solvent of low dissociating ability, this asymmetric coordination complex reacts with benzene diazo compounds through one-electron transfer only, without any azo coupling. By using THF as a solvent for both anion-radicals of *o*- and *p*-dinitrobenzenes, that is, under comparable experimental conditions, quite different products are obtained. As mentioned, the ortho isomer gives rise to the azo coupling product, whereas the para isomer is discharged as shown in Scheme 3.57.

In brief, the formation of a closed contour for the unpaired electron delocalization is a widespread phenomenon that detains the electron in the framework of a given molecular fragment and really defines the physical and chemical properties of ion-radicals.



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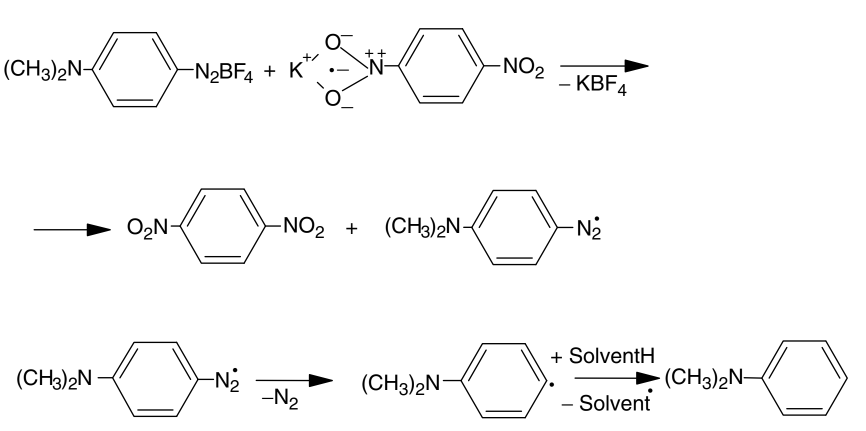


SCHEME 3.57

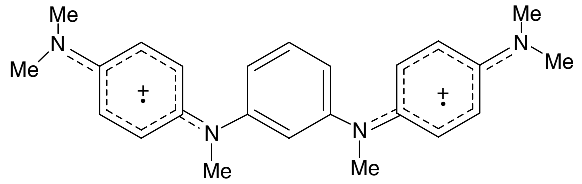
3.3 PRINCIPLE OF "RELEASED" ELECTRON THAT CONTROLS ION-RADICAL REACTIVITY

Ion-radicals of acyclic conjugated or aromatic hydrocarbons (butadiene or naphthalene) are typical examples of the species with a released unpaired electron. They are named π-electron ion-radicals and have spin distributions along the whole molecular contours. An important feature of such species is that all the structural components are coplanar or almost coplanar although ordinary bonds are usually contracted and double bonds are elongated. In this case, spin density appears to be uniformly or symmetrically distributed over the molecular framework. For instance, the central ordinary bond is strengthened in the butadiene cation-radical; meanwhile s-*cis* and s-*trans* forms do not become readily interconvertible. Spin density distribution also has a decisive effect on the thermodynamic stability of ion-radicals. When a LUMO or HOMO of a parent neutral conjugated molecule is nonsymmetrical, an unpaired electron occupies this orbital keeping its asymmetry. As a rule, the stability of ion-radicals increases with an enhancement in delocalization and in the steric shielding of the reaction centers bearing the maximal spin density. Blockading of the positions with high spin densities diminishes reactivity of ion-radicals and, to some extent, protects them from undesirable transformations.

For instance, the substitution of hydrogen atoms with the phenyl or methyl groups in active positions 9 and 10 of anthracene is a method for stabilizing the cation-radicals of 9,10-diphenyl- or 9,10-dimethylanthracene. Blockading of only one active position leads to a rather stable 9-phenylanthracene cation-radical, but to an absolutely unstable 9-methylanthracene cation-radical (Phelps et al. 1967). The phenyl group can delocalize a spin density more efficiently than the methyl group. It is worth noting, however, that the formation of hydrocarbon cation-radicals is rather difficult and demands high anodic potentials. Aromatic anion-radicals are achieved more readily.

In comparison with hydrocarbons, aromatic amines easily transform into cation radicals. Structures of these cation radicals are well documented on the basis of their ESR spectra and MO calculations (see, e.g., Grampp et al. 2005). The stable cation radical of *N,N,N′,N′*-tetramethyl-*p*-phenylenediamine (the so-called Wuerster's blue) was one of the first ion radicals that was studied by ESR spectroscopy (Weissmann et al. 1953). The use of this cation radical as a spin-containing unit for high-spin molecules has been reported (Ito et al. 1999). Chemical oxidation of *N,N′*-bis [4-(dimethylamino)-phenyl-*N,N′*-dimethyl-1,3-phenylenediamine with thianthrenium perchlorate in *n*-butyronitrile in the presence of trifluoroacetic acid at −78°C led to the formation of the dication diradical depicted in Scheme 3.58.

As seen, the spin–charge systems are disjoint in this paramagnetic species. The following two features of this dication-diradical are worth noting: It was found to be a triplet at ground state and



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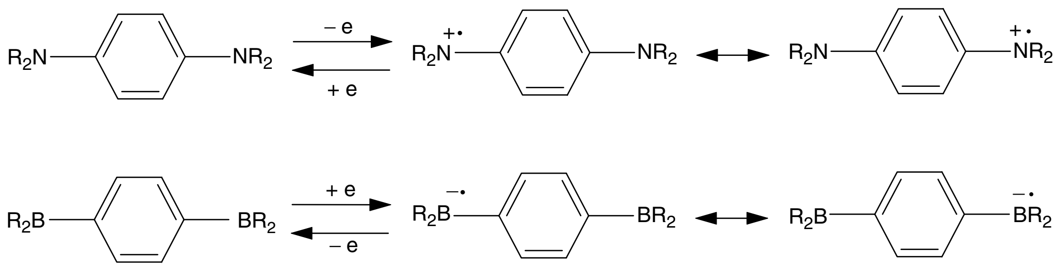


SCHEME 3.59

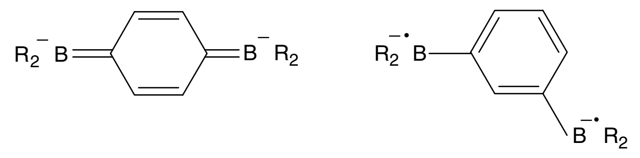
unstable at an ambient temperature. The methoxy group usually acts as a stabilizing substituent in amine cation radials. For example, *N,N*-dimethyl anisidine gives a stable cation-radical, whereas the *N,N*-dimethyl *p*-toluidine cation-radical is short lived, although its ESR spectrum can be recorded (Mann and Barnes 1970, Chapter 9). Deblockading of the para position sharply diminishes the cation-radical stability and enhances its reactivity. Thus, *N,N*-dimethylaniline and *N,N*-diethylaniline react with Cu^{2+} to form the corresponding amine cation-radicals. The cation-radicals were characterized by their UV-absorption spectra. In the absence of any nuleophiles, the cation-radicals dimerize to give *N,N,N′,N′*-tetraalkylbenzidines. In the presence of nucleophiles such as chloride, bromide, or thiocyanate, the cation-radicals undergo nucleophilic substitution to give para-substituted dialkylaniline in good yields (Kirchgessner et al. 2006).

Applying the concept of isoelectronic compounds and redox series proposed by Kaim (1980), one can point out the existence of analogous redox systems based on $-BR_2/-BR_2^{-\bullet}$ instead of $-NR_2/-NR_2^{+\bullet}$ as essential end groups of conjugated π systems. The corresponding redox series then involve anionic charges instead of cationic ones as seen in Scheme 3.59.

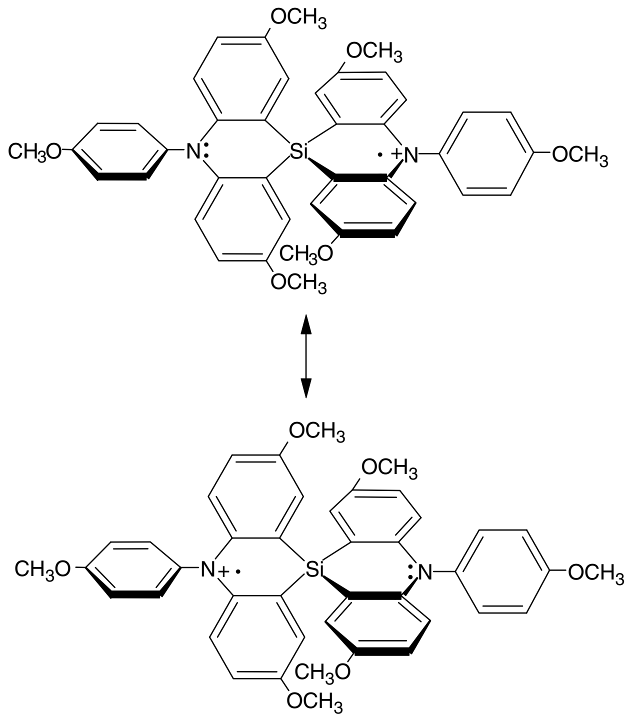
In the nitrogen and boron analogs depicted in Scheme 3.59, two methyl groups provide a sufficient shielding at the $NR_2^{+\bullet}$ centers (R = Me), whereas two mesityl groups are needed for the protection of $BR_2^{-\bullet}$ centers (R = 2,4,6-trimethylbenzene). Electrochemical studies of 1,4-bis(dimesitylboryl)benzene have shown two well-separated one-electron reduction processes, with the formation of the corresponding anion-radical and dianions, respectively (Fiedler et al. 1996). According to UV/visible/near-IR and ESR spectroscopic data confirmed by quantum-mechanical calculations, the unpaired electron primarily populates a $\pi(C_6H_4)$–$p_z(B)$-based MO (Fiedler et al. 1996). Resonance formulation foresees the participation of the central benzene ring (denoted as π) and both the boron atoms in the delocalization of an unpaired electron (a delocalized B^{III}/B^{II} mixed valence model).

$$[>B^{III}\text{–}\pi^{o}\text{–}B^{III}<] + e \rightarrow [>B^{III}\text{–}\pi^{o}\text{–}{}^{-}B^{II}<] \leftrightarrow [>B^{III}\text{–}\pi^{-\bullet}\text{–}B^{III}] \leftrightarrow [>^{-}B^{II}\text{–}\pi\text{–}B^{III}<]$$

Naturally, the product of two-electron reduction of the para derivative can be depicted (Scheme 3.60) as an anionic diborataquinoid system. In contrast to the *p*-diborataquinoid dianion, an anionic *m*-quinoid system is impossible. Indeed, the meta-substituted isomer depicted in Scheme 3.60 has been



SCHEME 3.60



SCHEME 3.61

characterized as a spin-unpaired triplet species with boron-centered spins (Rajca et al. 1995). This dianion-diradical can be viewed as two stable borane anion-radicals linked with a "ferromagnetic coupling unit," that is, 1,3-phenylene (see Chapter 1).

In addition, it should be useful to mention that silicon as a spiro atom is able to conjugate its mutually orthogonal aromatic constituents, and thus, secures a release of an unpaired electron in a cation-radical. Scheme 3.61 shows such a phenomenon, revealed by Hirao et al. (2007). Obviously, vacant *d* orbitals of silicon provide the cation-radical with the possibility of delocalizing spin density.

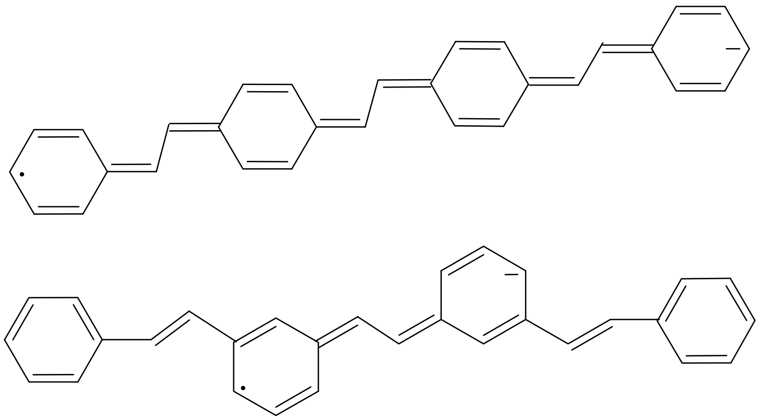
3.3.1 Effects of Spread Conjugation in Ion-Radicals Derived from Molecules with Large Contours of Delocalization

Attention should be paid to the fact that the electron motion from a donor to an acceptor or within spread-conjugated ion-radicals generates measurable electromagnetic radiation. In other words, there is one specific way to reveal intramolecular electron motion or intermolecular electron transfer in charge-transfer complexes. To probe electron transfer in this manner, the only fundamental requirements are that the molecule can be oriented in the external magnetic field. This takes place most easily if the species considered has a ground state dipole moment. On photoexcitation, there

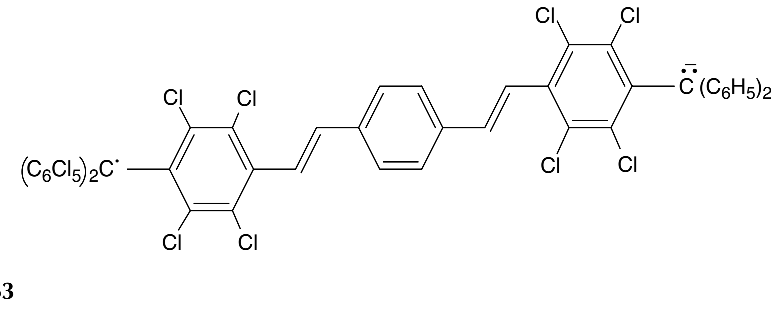
is a change in the dipole moment along the molecular axis of orientation. The sign of the radiated electromagnetic field depends on whether the change in dipole is positive or negative. For example, on photoexcitation at 400 nm of 4-dimethylamino-4-nitrostilbene dissolved in toluene, the dipole moment of the stilbene increases. This corresponds to the amino-to-nitro electron transfer. Thus, the direction of the electron transfer can be determined directly from the electromagnetic measurement (Beard et al. 2000). An unpaired electron and charge can be spread over the whole molecule or localized with one conjugated part (see Scheme 3.62).

The anion-radicals depicted in Scheme 3.62 were investigated by ESR and electron adsorption spectroscopy (Gregorius et al. 1992). The para isomer appears to behave completely different from the meta isomer. In full agreement with the results from MO theoretical calculations, the unpaired electron is delocalized over the whole para isomer, but confined to a stilbene unit in the meta isomer. The remaining parts in the meta isomer are uncharged. This spontaneous charge localization is not a consequence of steric hindrance, but follows from the role of the *m*-phenylene unit as a conjugational barrier.

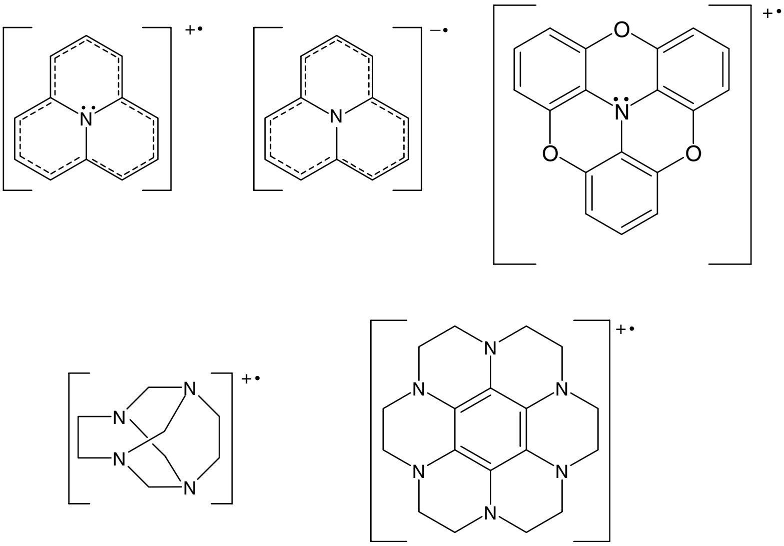
In a similar manner, *p*-bis(9-anthryl) phenylene gives a mono(anion-radical) or a mono(cation-radical) under reductive or oxidative conditions with spin delocalization around the whole molecular framework. In the case of *m*-bis(9-anthryl) phenylene, reduction or oxidation leads to the formation of dianion or dication-diradicals. Based on ESR experiments at cryogenic temperatures (6.5–85 K), these species contain two separated ion-radical moieties. They have parallel alignment of their spins (Tukada 1994). The work gives clear experimental evidence for the so-called ferromagnetic interaction between these ion-radical substituents. In some cases, release of the electron depends on temperature. See, for example, the anion-radical shown in Scheme 3.63.



SCHEME 3.62



SCHEME 3.63



SCHEME 3.64

The stable anion-radical in Scheme 3.63 contains two perchlorotriphenylmethyl radical units linked by an all-*trans*-*p*-divinylbenzene bridge. At 200 K, the unpaired electron of the anion-radical is localized (within the ESR timescale) on one stilbenelike moiety only. At 300 K, thermal activation forces the unpaired electron at one strong electrophilic center to move to another one. Such an electron transfer takes place between two equivalent redox sites (Bonvoisin et al. 1994). In contrast to this situation, no electron transfer was observed for the anion-radical that contains two perchlorotriphenylmethyl radical units linked by an all-*trans*-*m*-divinylbenzene bridge (Rovira et al. 2001). Such results can be ascribed to the localization of frontier orbitals in the meta-isomeric anion-radical because of the meta connectivity of this non-Kekule structure.

There are special cases when the ring contour of delocalization is organized immediately after the transition of neutral molecules into ion-radicals; the four relevant examples are depicted in Scheme 3.64. The first example belongs to the cyclo[3.3.3]azine molecular system. In this compound, the central nitrogen atom bears a lone electron pair. Oxidation by silver perchlorate or silver fluoroborate in DMF leads to the cation-radical. It is logical to presume that an electron should be removed from the lone electron pair at the central nitrogen. As a matter of fact, the formation of a peripheral π-electron system takes place. Therefore, the central nitrogen atom presumably keeps the peripheral system planar and its lone electron pair contributes very little to the peripheral conjugation. By means of SCF-MO calculations and ESR experiments, both cation-radical and anion-radical of cyclo[3.3.3]azine are aromatic with no essential double bond localization (symmetry D_{3h}). This is in contrast to the neutral compound that exhibits alternating essential single and double bonds (symmetry C_{3h}). In the ion-radical, the central nitrogen atom is presumably coplanar with the twelve-membered rings (Dewar and Trinajstic 1969, Gerson et al. 1973). The electron distribution in these ion-radicals is not time dependent, and the peculiarities discussed earlier should not be understood as involving an electron released from the nitrogen atom.

The second example depicted in Scheme 3.64 is the trioxotriphenylamine cation-radical. Kuratsu et al. (2005) compared structures of the cation-radical and its neutral counterpart. The neutral compound has a shallow bowl structure, whereas the cation-radical has a planar structure. In the latter, spin delocalization embraces a whole molecular contour, involving the oxygen atoms. This contributes to the cation-radical stability. (The solid species is easily formed after oxidation of the neutral parent compound with tris(*p*-bromophenyl)aminiumyl hexafluorophosphate in methylene

chloride. The solid species can be recrystallized; in solution, it suffers neither dimerization nor oxygenation under aerated conditions. For these reasons, such compounds have potential applicability in electronic and magnetic materials.)

The third example in Scheme 3.64 represents the cation-radical of 1,3,6,8-tetraazatricyclo [4.4.1.1^{3,8}]dodecane. Zwier et al. (2002) produced evidence of instantaneous electron delocalization over the four equivalent nitrogen atoms. This extensive delocalization in a completely saturated system is a principal feature of the third example and reveals the consequences of orbital interactions through space and bonds. The space–bond delocalization can serve as a driving force for the cation-radical rearrangements as it has recently been exemplified by transformation of the phenylhousane cation-radical into a mixture of phenylbicyclononenes (Gerken et al. 2005).

The fourth example in Scheme 3.64 puts forward the most stable cation-radical of hexaaza-octadecahydrocoronene (Miller et al. 1990). This cation-radical is characterized by effective spin delocalization with the participation of all its six nitrogen atoms. Interestingly, the parent neutral compound gives not only the cation-radical, but also the dication, tri(cation)-radical, and even tetracation. All of these cationic forms are stable and their crystal structures were described.

Related compounds, cyclo[2.2.3]azine and 1,2,3,4-dibenzocyclo[2.2.3]azine, also give ion-radicals with peripheral π-electron conjugate systems (Gerson et al. 1973, Matsumoto et al. 1996).

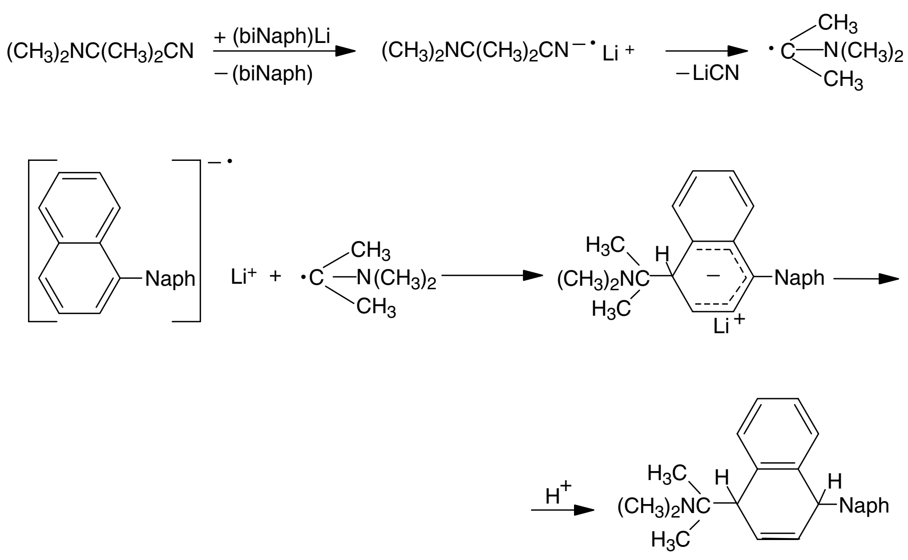
The difference in conjugation between neutral molecules and their ion-radicals can also be traced for keto-enol tautomerism. As a rule, enols are usually less stable than ketones. Under the equilibrium conditions, enols exist only at a very low concentration. However, the situation becomes different in the corresponding cation-radicals, where gas-phase experiments have shown that enol cation-radicals are usually more stable than their keto tautomers. This is because enol cation-radicals profit from allylic resonance stabilization that is not available to ketones (Bednarek et al. 2001, references therein).

$$(R_2CH{-}CH{=}CH{-}C(R){=}O)^{+\bullet} \rightarrow (R_2C{=}CH{-}CH{=}C(R){-}OH)^{+}$$

3.3.2 Spin Delocalization in Ion-Radicals Derived from Molecules of Increased Dimensionality

Sometimes transformation of aromatic compounds into ion-radicals leads to stereochemically unusual forms. Octamethylnaphthalene is a nonplanar molecule twisted around the bond that is common for the two six-membered rings. The nitrosonium oxidation results in the formation of the cation-radical with the centrosymmetric flatten chairlike geometry (Rosokha and Kochi 2006). According to the authors, such a skeletal transformation improves the overall planarity of octamethylnaphthalene. For example, the mean deviation of the carbon atoms in the naphthalene core for the flatten chairlike cation-radical (0.007 nm) is less than half of the corresponding value for the neutral twisted parent (0.016 nm). Within this flatten carcass of the anion-radical, the spin density can be delocalized more effectively.

On being converted into the anion-radical state and then oxidized, enantiomeric binaphthyls return as a racemic mixture. Let us scrutinize causes of this racemization. In a neutral 1,1′-binaphthyl, the most stable conformation is the one in which the naphthalene rings forms an angle of 70°. This results in a very small π overlap and the existence of two enantiomers (atropoisomers), differing in the arrangement of one naphthyl nucleus above or below the plane of the other. Following transformation into the anion-radical state, 1,1′-binaphthyl acquires a stereochemically unusual form in which the torsion angle is reduced to about 50° (Baumgarten et al. 1995). This permits complete delocalization of the unpaired electron and leads to a loss of chirality. Steric strains inherent in the conformation of the newly formed are compensated for by the gain in the delocalization energy: The unpaired electron may be distributed on two naphthyl nuclei instead of only one. On one-electron oxidation, the anion-radical of 1,1-binaphthyl loses planarity and should produce a mixture of enantiomers. According to the calculations (Eisenstein et al. 1977),



SCHEME 3.65

when the anion-radical of binaphthyl acquires an almost planar conformation, the number of most reactive sites decreases from three (positions 4,5, and 8) to one (position 4). Carbon-4 has the greatest electron density. This has been confirmed by the ESR data (Eisenstein et al. 1977, Baumgarten et al. 1993). Indeed, the ion-radical reactions of binaphthyl proceed nonstereospecifically, but regioselectively. On treatment of one enantiomer (in tetrahydrofurane) with lithium and then with aminonitrile, aminoalkylation is strictly directed to the position 4 of the naphthalene fragment. The part of binaphthyl that does not participate in alkylation, returns in the optically inactive form (Eisenstein et al. 1977; Scheme 3.65).

The final stage of the reaction in Scheme 3.65 involves protonation, yielding the derivative of 1,4-dihydronaphthalene. The oxidation may produce a 4-substituted binaphthyl, which is not contaminated with the isomeric products. It is worth noting here that the described ion-radical method of introduction of the alkyl group into the aromatic nucleus has an advantage over the radical or heterolytic alkylation. In these cases, the neutral substrate may produce a composite mixture of isomeric products. The binaphthyl anion-radical reaction proceeds regioselectively and nonstereospecifically.

Conformational features of the binaphthyl anion-radical are also observed for the cation-radical. Desmarets et al. (2006) theoretically and experimentally studied the cation-radical and dication-diradical from *N*,*N*′-bis(*p*-anisyl)-4,4′-dinaphthyl-1,1′-diamine. For example, both naphthyl groups are turned by ca. 75° in the initial uncharged molecule and only by 55° in the cation-radical. The conformation change results from the one-electron oxidation. According to the electrochemical data as well as ESR and UV spectra, intramolecular spin distribution is observed over the whole molecular contour of the cation-radical. Surprisingly, the second oxidation leads to the dication-diradical, in which both naphthyl groups appeared to be turned by about 70°. It means that the second one-electron oxidation almost restores the large torsion angle of the starting binaphthyl diamine. In the case of the dication-diradical, each naphthyl amine unit carries an unpaired electron separately. The authors deemed the dication-diradical as a species having a pair of independent cation-radical moieties in the doublet spin state.

The ethylene cation-radical is significantly twisted by approximately 25–40°, according to different estimations. The twisting is necessary for an overlap to occur between the ethylenic bond and the *p* orbital bearing a spin (and a charge). The untwisted system has no hyperconjugative stabilization. As the degree of substitution increases, enabling hyperconjugative stabilization from the

substituents, the degree of twisting is reduced. There is basically no barrier for the twisting in the ethylene cation-radical, but in the cation-radical of 1,2-dimethyl derivative the cis and trans isomers occur to be different, and are characterized with a high barrier for the interconversion (Clark and Nelsen 1988). The tri(methyl) and tetra(methyl) ethylene cation-radicals are essentially planar (Crich et al. 2006).

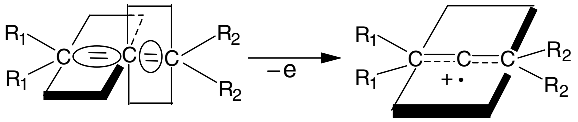
The allene molecule resembles binaphthyl in terms of its two cumulated π systems and the orthogonality of these system planes. (A quantum mechanical model of cumulative double bonds in allenes forecasts sp^2 electron state for both terminal carbon atoms. The central carbon atom has *sp* hybridization. Therefore, the bond system, which proceeds from this central atom, is linear. Both double bond and terminal substituents are located in mutually perpendicular planes.) Both neutral allene and its cation-radical are depicted in Scheme 3.66. In the allene cation-radical, the angle between the double bond planes is diminished and reaches 30–40° (Takemura and Shida 1980). According to calculations (Hasselbach 1970), a multiatomic linear cation-radical of allene has a degenerate electron state. Indeed, in accordance with the Jahn–Teller theorem, this cation-radical should undergo distortion of the geometry to acquire a less symmetric form. As calculations show (Takemura and Shida 1980, Somekawa et al. 1984), the most favorable form is the one with an angle between the ethylene bond planes of ca. 40°. The allenic group (>C=C=C<) is a moderate π donor (Nagase et al. 1979).

The allenes bearing four *tert*-butyl or four trimethylsilyl groups at the terminal carbons react in dichloromethane with antimony pentachloride. The cation-radicals formed contain an unpaired electron delocalized along the neighboring π bonds. The conclusion is based on the analysis of ^{1}H, ^{13}C, and ^{29}Si ESR spectra (Bolze et al. 1982), as well as on photoelectron spectra (Elsevier et al. 1985, Kamphius et al. 1986). These data were confirmed by Werst and Trifunac (1991) in a further study. The spectrum of this cation-radical was observed by fluorescent-detected magnetic resonance. The well-resolved multiplet due to this cation radical consists of a binomial 13-line pattern owing to 12 equivalent methyl protons. This is in full accordance with Scheme 3.66.

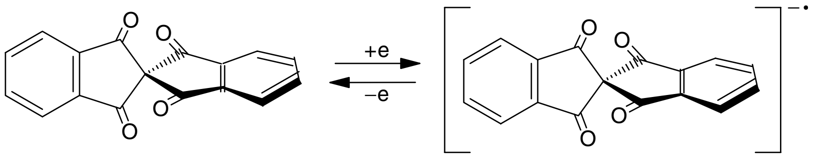
As proven, a fundamental difference was found between allene (cumulated double bonds are separated in the space) and the allene cation-radical (cumulated double bonds are conjugated and lay at the same plane).

Spiro compounds are known to have joined rings in two perpendicular planes with a nodal common atom. This atom (the quaternary carbon) can prevent conjugative interactions between the two joined rings. In the case of two identical orthogonal π networks joined by a spiro atom, the orbitals of the "halves" may interact only if they possess the same symmetry. Such interactions lead to pairs of delocalized orbitals encompassing the entire molecule. This is a realization of the spiroconjugation phenomenon (for a review of spiroconjugation, see Durr and Gleiter 1978).

Spiro-bis(indanedione) from Scheme 3.67 is one example of this kind of conjugation. Moreover, its frontier orbital (LUMO) also satisfies the symmetry requirement mentioned here. Hence, it can



SCHEME 3.66



SCHEME 3.67

be formally considered as a bonding combination of the "half-molecule" orbitals (Maslak et al. 1990). Spiro-bis(indanedione) was reduced with anion-radicals of polyaromatic compounds serving as electron donors at low temperatures (195–173 K). An anion-radical of the spiro compound was formed. When treated with dioxygen, this anion-radical gave the starting, unchanged dione (Scheme 3.67).

The spiro(indanedione) anion-radical in Scheme 3.67 was studied by ESR and UV/visible spectroscopy (Maslak et al. 1990). The spectra clearly indicated delocalization of the spin density over the entire molecular framework. An unpaired electron undergoes simultaneous delocalization between the halves (in the ESR timescale). The observed spectra were independent of the counterions (Li^+, Na^+, and K^+), thus excluding any ion-pairing complication. As a general inference, an unpaired electron spends its time on both the half-shaped orbitals with no geometrical changes in the molecular skeleton of this anion-radical.

Simultaneous delocalization of an unpaired electron over two molecular halves is caused by rapid electron transfer. Ballester et al. (1991) described another example of such a transfer with no geometrical changes in the molecular skeleton. In $(C_6Cl_5)_2C^{\bullet}{-}C_6Cl_4{-}C_6Cl_4{-}C^{\pm\bullet}(C_6Cl_5)_2$, there is a very rapid intramolecular electron transfer between radical and ion-radical sites. Repulsion among the four chlorine atoms ortho located with respect to the central liaison ($-C_6Cl_4-C_6Cl_4-$) causes the two phenyl rings of the biphenyl system to be perpendicular to each other. On account of this perpendicularity, the authors conclude that "the overlap involving the higher energy bonding π orbitals is practically nonexistent in these ion-radicals…. Therefore, at least some spin–charge described here take place along the σ path."

A significant subject is the involvement of the ion-radicals' counterions ($SbCl_6^-$ or $(n\text{-Bu})_4N^+$) in the exchange process. According to the experimental conditions employed, the authors had the free ion-radicals, exclusively. Hence, the counterion did not appear to play any important role in the spin–charge alternation. It is some kind of σ conjugation, which also plays a role in delocalization (or releasing) of an unpaired electron in ion-radicals.

3.4 BIOMEDICAL ASPECTS OF ION-RADICAL ORGANIC CHEMISTRY

3.4.1 Cation-Radical Damage in Deoxyribonucleic Acid

A substantial body of experimental evidence indicates that the formation of a covalent bond between chemical carcinogens and cellular macromolecules represents the first critical step in the multistage process, eventually leading to tumor formation (see Geacintov et al. 1997, references therein). Most chemical carcinogens are not active on their own, but require metabolic activation to produce reactive intermediates capable of binding covalently with target macromolecules, particularly with deoxyribonucleic acid (DNA), and thereby, initiate cancer.

The most widespread of environmental carcinogens are the polycyclic aromatic hydrocarbons (PAHs), which are found, among other places, in automobile exhaust, cigarette smoke, and broiled meats. PAHs undergo two main pathways of bioactivation: one-electron oxidation and oxygenation. The former yields cation-radicals; the latter produces hydroxyl derivatives. One-electron oxidation to form cation-radicals is the major pathway of activation for the most potent carcinogenic PAHs, whereas oxygenation is generally a minor pathway. For benz[a]pyrene and 7,12-dimethyl benz[a]anthracene, 80 and 90%, respectively, of the DNA adducts formed by rat liver microsomes or in mouse skin, arise via the cation-radicals (Cavalieri and Rogan 1992).

One-electron oxidation of PAHs to form cation-radicals is a coexistent mechanism of activation, which can account for the binding of the most potent hydrocarbons to DNA and, presumably, for their carcinogenic activity. These reactive electrophiles are produced by removal of a π electron by the biological oxidant P450 (Cavalieri et al. 1988a, 1990) and peroxidases such as prostaglandin H synthase and horseradish peroxidase (Cavalieri et al. 1988a, Rogan et al. 1988, Rogan et al. 1979).

The reason that one-electron oxidation is suggested as playing a central role in the metabolic activation of PAHs concerns certain features of the cation-radicals that are common to the most potent carcinogens of the family.

1. Relatively low IP, which allows metabolic removal of one electron with the formation of a relatively stable cation-radical
2. Charge localization in the cation-radical that renders this intermediate specifically and efficiently to react with nucleophiles
3. Optimal geometric configuration that allows the formation of appropriate intercalating physical complexes with DNA, thus favoring metabolic activation and the formation of covalent bonds with DNA nucleophiles

All these factors are specifically important in carcinogenesis. Therefore, it is worthwhile considering them separately from the general regularities of the formation and stability of organic ion-radicals.

3.4.1.1 Ionization Potentials of Carcinogens

The ease of formation of PAH cation-radicals is related to their IP. Above a certain IP, activation by one-electron oxidation becomes unlikely because the removal of one electron by the active forms of P450 or peroxidases is more difficult. A cutoff IP above which one-electron oxidation in not likely to occur was tentatively proposed to be about 7.35 eV (Cavalieri and Rogan 1995). For example, 7,12-dimethylbenz[a]-anthracene has an IP of 7.22 eV and is extremely carcinogenic. Benz[a]anthracene has an IP of 7.54 eV and is very weak in this sense. The active carcinogenicity of dibenz[a,h]anthracene (IP 7.61 eV) is not attributable to the one-electron mechanism. It is worth noting that the one-electron transfer is only one of the operating mechanisms of carcinogenesis.

3.4.1.2 Localization of Charges and Spins in Cation-Radicals of Carcinogens

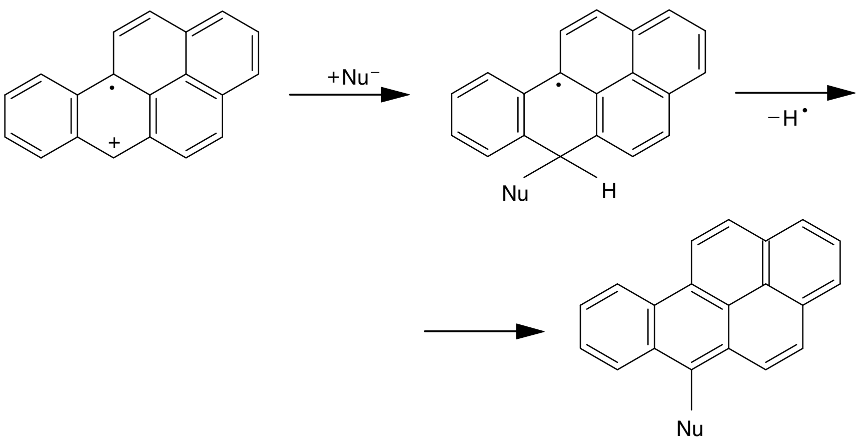
A relatively low IP is a necessary, but not sufficient, prerequisite for activating PAHs by one-electron oxidation. Another important factor that must be combined with IP to predict carcinogenic activity through this mechanism is charge localization in a PAH cation-radical. Specificity in cation-radical reactivity derives from the relative localization of charge at one or a few carbon atoms.

In situ generation of these cation-radicals has been used in their identification as biological metabolites. A valid alternative was to synthesize the cation-radical as a solid salt, isolate it, and investigate its reactions with various nucleophiles including DNA. Such studies were conducted to better understand the role of those intermediates in biological systems (Murata and Shine 1969, Ristagno and Shine 1971, Cremonesi et al. 1994, Stack et al. 1995).

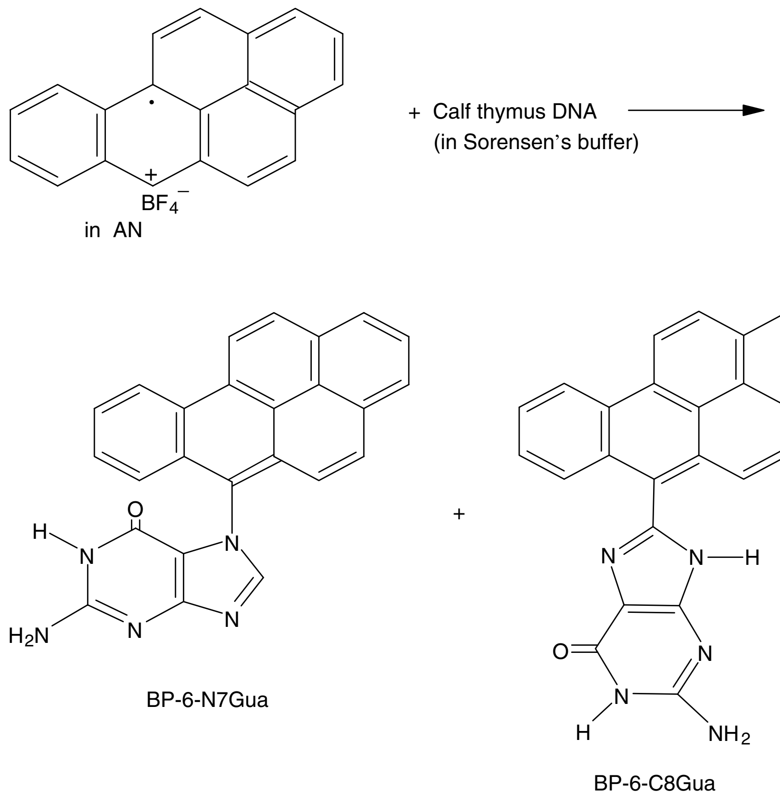
For instance, $NOBF_4$ oxidation of benzo[*a*]pyrene (BP, the additional benzene ring is fused at positions 7 and 8 of pyrene) generates the $BP^{+\bullet}BF_4^-$ salt. When this cation-radical salt is attacked with nucleophiles of various strengths, the pattern of nucleophilic substitution reflects the distribution of a positive charge in the cation-radical part of the salt. This positive charge is localized mainly at the *meso*-anthracenic position, that is, at the C-6 atom. Nucleophiles (Nu^-) such as OH^-, AcO^-, and F^- enter this position (Scheme 3.68).

The reaction of $BP^{+\bullet}$ with DNA produces two derivatives, BP-6-N7Gua and BP-6-C8Gua, originating from the depurination of DNA (Stack et al. 1995). The derivatives are depicted in Scheme 3.69.

When binding of the uncharged BP with DNA is catalyzed by horseradish peroxidase (Cavalieri et al. 1988b) or rat liver microsomes (Cavalieri et al. 1988a), the same pattern of the DNA-depurinating BP derivatives was obtained. As mentioned earlier, horseradish peroxidase activates BP by one-electron oxidation, hence, this result is just as expected (Rogan et al. 1979, 1988).

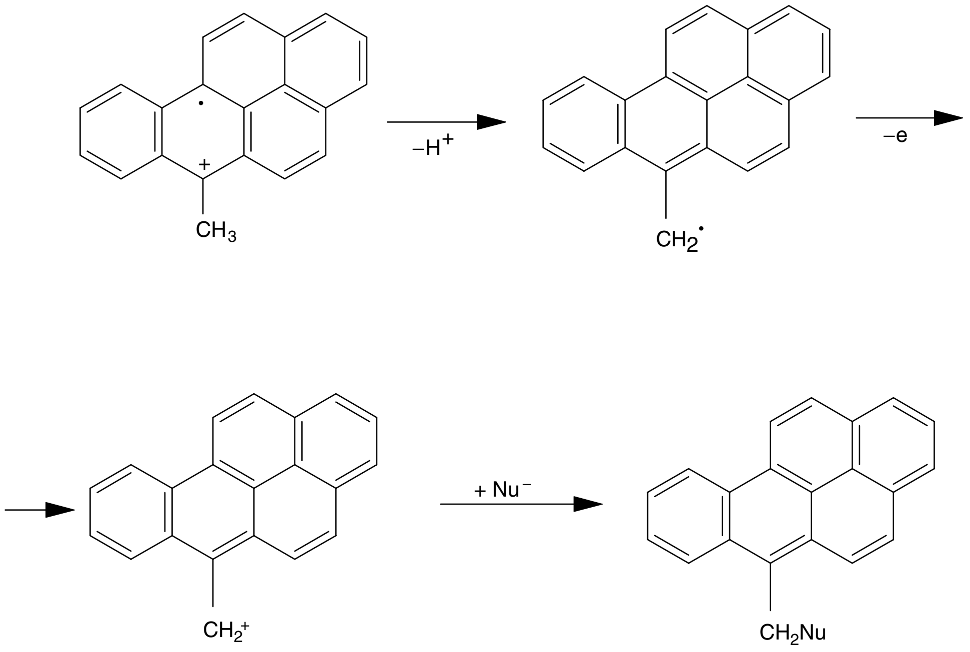


SCHEME 3.68



SCHEME 3.69

If a carbon atom bearing a positive charge is bound with the methyl group, the reaction path consists of a methyl proton loss. This is the intrinsic property of methyl derivatives in the cation-radical state. The deprotonation generates a benzylic-type radical that is rapidly oxidized to a so-called benzylic carbocation, which reacts with a nucleophile as shown in Scheme 3.70. From Scheme 3.70 it is clear that BP-6-methyl can act as an active carcinogen (Cavalieri and Rogan 1995).



SCHEME 3.70

When the positive charge in the cation-radical is adjacently localized to the ethyl group, such as in 6-ethyl-BP, a reaction cannot occur at the "benzylic" methylene group. The reason is a less favorable alignment of CH_2 fragment in CH_2CH_3 group with the π system to cause deprotonation when compared to the C–H bond of CH_3 group. This ethyl-substituted BP is noncarcinogenic (Cavalieri and Rogan 1995).

Meanwhile, nucleophile activity in the interception of a cation-radical is also an important factor. For example, 7,12-dimethyl-benz[a]anthracene (DMBA) is oxidized with iodine in the presence of pyridine, yielding methylene pyridinium derivatives at the methyl groups in the positions 7 and 12. At the same time, the ring position 5 also participates in the reaction. Acetate ion is a weaker nucleophile than pyridine. Therefore, when DMBA is oxidized with manganese acetate in acetic acid, only the acetoxy derivatives at the 7-CH_3 and 12-CH_3 groups are obtained. The same exclusive methyl substitutions occur with weak nucleophiles such as adenine and guanine to produce substitution products when DMBA is electrolytically oxidized in the presence of deoxyadenosine or deoxyguanine (Cavalieri and Rogan 1995). Similarly, BP cation-radicals show lesser selectivity with stronger nucleophiles, but higher selectivity with weaker nucleophiles. This feature of regioselectivity is cardinally significant for biochemical reactions.

3.4.2 On Geometrical and Spatial Factors Governing the Behavior of Ion-Radicals in Biological Systems

Another important factor affecting the ability of PAH cation-radicals to elicit carcinogenic activity is their shape and size. Generally, carcinogenic activity is found in PAHs that contain three to seven condensed rings. A more stringent requirement concerning geometric features of PAHs is the presence of an angular ring in the benz[a]anthracene series. This ring is necessary for eliciting the carcinogenic activity regardless of the ring being aromatic or alicyclic. One-electron oxidation of PAHs gives cation-radicals with no changes in precursor geometry. As noted (Cavalieri and Rogan 1995), the DNA adducts with the cation-radicals of benzopyrene and DMBA can be obtained only

from double-stranded DNA (animal DNA), but not from single-stranded DNA (bacterium DNA). According to Geacintov et al. (1997), metabolites of PAHs bind to the purine bases in DNA to form adducts, which intercalate between bases in the DNA double helix.

By locally stretching and unwinding the helix, the metabolite can slip between pairs of bases in the DNA double helix without displacing any of these bases. DNA treated with PAH cation-radicals contains relatively large amounts of apurinic sites, as well as some stable adducts. Enzymes, many of which move along the polymeric strand in a particular direction, process DNA. Thus, the enzymes will see damaged parts of DNA (depurinated or stretched and unwound) and provoke tumorigenic replications. Of course, particular DNA sequences are more prone to mutation than others. These "hot spots" vary in different organisms. PAH cation-radicals can serve as a useful tool to study this particular problem.

At this point, it is expedient to give some intermediate inference. As mentioned in Section 3.4.1, there are two principal mechanisms of bioactivation: oxygenation and one-electron oxidation. Recently, the scientific community has considered oxygenation to be the exclusive mechanism of carcinogenesis from PAH (see, e.g., Hall and Grover 1990). The arranged material involves one more, and obviously, main mechanism of the PAH carcinogenic effect. The formation of PAH cation-radicals plays the central role in such a mechanism. These PAHs generally have relatively low IPs. They give cation-radicals with an expressed localization of a spin and a charge. Oxygenation to form bay-region diol epoxides is generally a minor, reserve pathway. For instance, benz[c]phenanthrene cannot effectively generate its cation-radical in the common biological condition of oxidation. It has a relatively high IP. In this case, the only possible pathway of carcinogenic activation is the formation of its diol derivative.

It is worth mentioning that the cation-radical mechanism of carcinogenesis was established for readily oxidizing PAHs that belong to a series of alternant aromatics. Nonalternant PAHs remain an attractive field for future exploration. Hydrocarbons with condensed aromatic rings containing at least one ring with an odd number of skeletal atoms can be pinpointed as possible candidates for such a study. Benz[j]fluoranthene, benz[k]fluoranthene, and benz[c, g]carbazole were named as desirable examples (Cavalieri and Rogan 1992). Hydrocarbons, which has been qualified by Balaban and Schmalz (2006) as *antisextet dualists of sextet-resonant benzenoids* are also a challenge. One very intriguing work on benz[c]acridines and benzo[a]phenothiazines established a connection between their carcinogenicity and radical production (Kurihara et al. 1998). It would be interesting to check for a connection between the carcinogenicity and electronic structures of the corresponding cation-radicals, too.

The aforementioned behavior of P450 as a one-electron oxidant needs to be explained. Since P450 is overall a two-electron oxidant, it is *a priori* unbelievable that this enzyme would release a highly reactive cation-radical from its active site. The authors cited in the following text considered different aspects of such unexpected resistivity of cation-radicals to further oxidation.

Rogan et al. (1988), and later Cavalieri et al. (1990) suggest that the cation-radical pathway may represent a nonactive site, a "heme-edge" oxidative process, which is akin to that observed for reactions between peroxidases and PAHs having low oxidation potentials. As already mentioned, a double helix DNA is able to stabilize PAH cation-radicals. It is also capable of stabilizing cation-radicals of other xenobiotics. For instance, chloropromazine is also oxidized to its cation-radical form by peroxidases. Double helix DNA stabilizes this cation-radical due to intercalation into the helix (Kelder et al. 1991). The intercalation enhances the stability of the chloropromazine cation-radical. It is suggested (Piette et al. 1964) that this inner-cell intercalation prevents further oxidation of the cation-radical. In model experiments, oxidations of chloropromazine and related phenazines in the cavity of cyclodextrins as a result of one-electron oxidation by iodine in aqueous solutions stop after the formation of the corresponding cation-radicals (Guo et al. 1992). Chloropromazine and related phenazines have significant physiological activity (mostly due to their neuroleptic properties) and are used as tranquilizers. They have low IPs and can act as good electron donors.

The problem of spatial specificity concerning the ion-radical binding in biological surroundings also need to be considered separately. Thus, phenothiazines may act in living organisms as electron-transfer donors at drug receptor sites. Some mechanisms of biological activity directly involve stable cation-radicals of the chloropromazine-type drugs (Gooley et al. 1969). As shown, the cation-radicals of this type have generated a somewhat flattened structure when compared to the corresponding neutral molecules. Therefore, the cation-radicals have increased aromatic resonance stabilization (Pan and Phillips 1999). Meanwhile, these cation-radicals remain somewhat bent in their skeleton. The chlorine atom at the position 2 in chloropromazine appears to be in noticeable conjugation or in through-bond interactions with the central ring heterocycle (Pan and et al. 1999, 2000). This seemingly affects the donor ability of the drug and its pharmacological activity. Although chloropromazine is about an order of magnitude more toxic than promazine (Merville et al. 1984), chloropromazine is still used as a psychotropic drug. What is important for our consideration is that the variation of the dihedral angle accompanying the transformation of neutral molecules into their cation-radicals may play an important role in the pharmacological activity of the drugs.

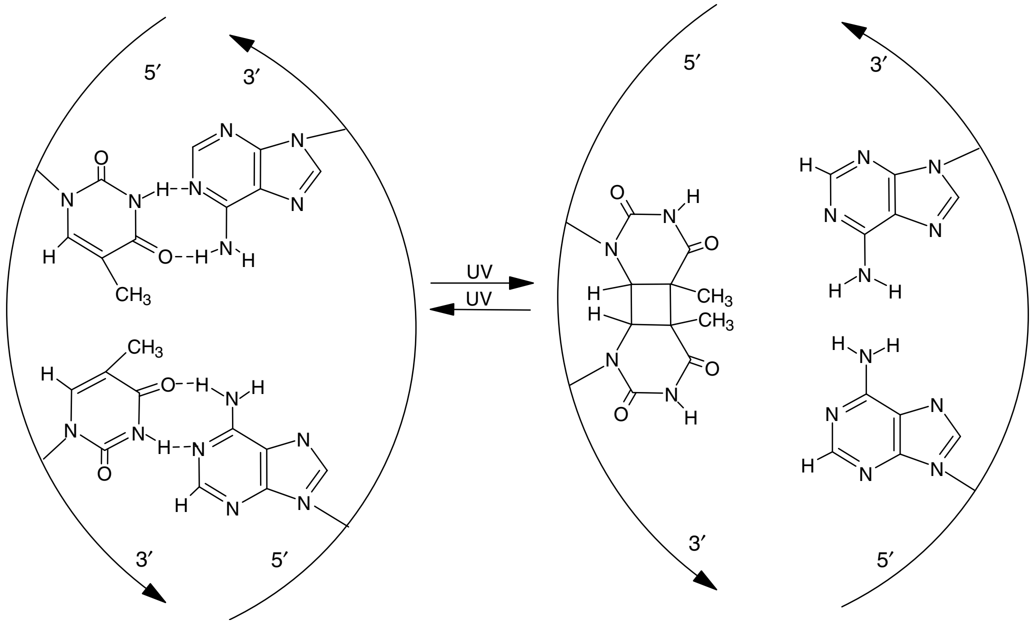
Anion-radical generation is also accompanied by conformational changes in biomolecules; the anion-radicals of the ubiquinone family can be illustrated as follows. Ubiquinones belong to Q_n coenzymes; they are 2,3-dimethoxy-5-methyl-6-poly(prenyl)benzoquinones. The prenyl group means an isoprene (3-methylbut-2-en-iso-yl) unit; the *n*-index represents the number of prenyl units. The Q_6–Q_{10} coenzymes are prevalent in nature; the ubiquinone name was coined to indicate their ubiquitous presence in nature. All of them have the *E* configuration of the prenyl units. The Q_{10} coenzyme is found in humans. The main biological function of Q_n coenzymes consists of electron and proton transfers from different substrates to cytochromes during respiration (breathing) and oxidative phosphorylation. As shown, after the electron uptake, both methoxy groups in positions 2 and 3 align in an out-of-plane orientation and reside on the same side of the six-membered ring plane (Himo et al. 1999).

Thus, the C-2 methoxy group in ubiquinone is found to orient differently in the neutral and in the anion-radical molecular system. This electron-induced conformational modification may cause a modified influence from surrounding hydrogen-bonding groups to the anion-radical. Proteins bind enzyme by means of hydrogen bonding. Formation of hydrogen bonds modifies the quinone electron affinity (Eriksson et al. 1997). As a result, it modifies the quinone ability for electron donation/uptake and proton uptake relative to the neutral system. Calvo et al. (2000) studied the electron-exchange interaction and the electron-transfer rate between two anion-radicals of ubiquinone, considering them as participants of photosynthetic reaction centers in *Rhodobacter sphaeroides*. The protein medium surrounding these semiquinones appeared to be especially favorable for the electron exchange. The medium extends the distance for which the electron transfer remains possible.

In principle, quinones can generate both cation and anion-radicals being involved in redox cycles of living organisms. The question of which reactive species—cation- or anion-radical—is responsible for genotoxic activity, has been the subject of special investigations. For example, 3,4-estrone quinone is capable of inducing single-strand DNA breaks in MCF-7 breast cancer cells. Akanni and Abul-Hajj (1999) carried out studies on the reactivity of the quinone, its cation- and anion-radicals with calf thymus DNA under variable pH conditions. Their results suggest that the reactive species responsible for adduct formation under physiological conditions is most likely to be the 3,4-estrone quinone anion-radical (SQ).

3.4.3 Ion-Radical Repair of Damaged Deoxyribonucleic Acid

Some ion-radical mechanisms are implicated in the DNA damage; others can be described as repairing the damage. In normal DNA, bases belonging to the two opposite strands are bound by relatively weak hydrogen bonds. In case of complementary base pairs, several hydrogen bonds are formed; they are depicted in Scheme 3.71.

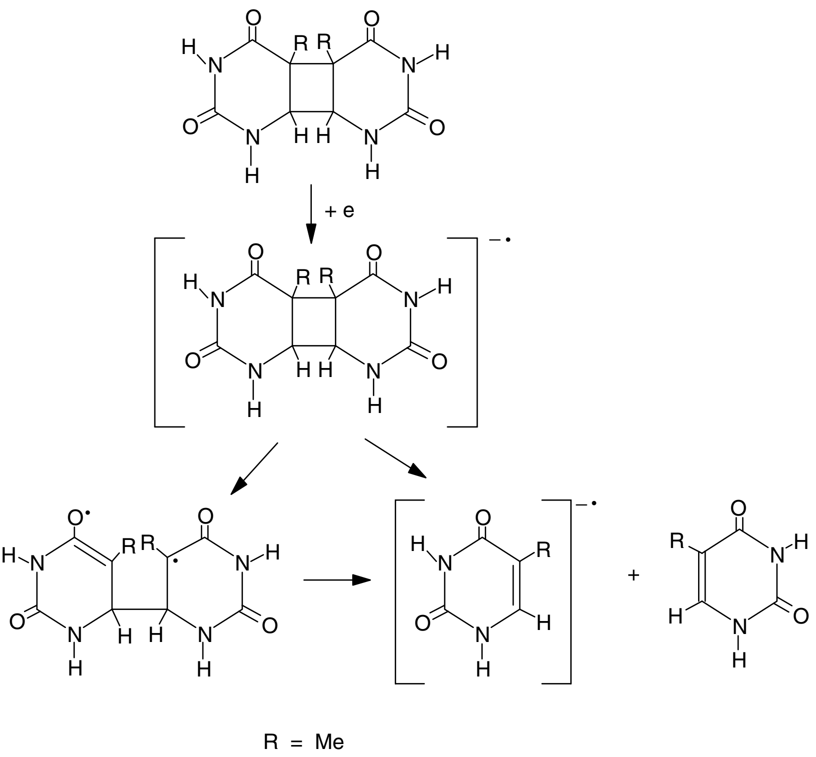


SCHEME 3.71

As shown in Scheme 3.71, there are two hydrogen bonds between the thymine and adenine bases. On photoirradiation (in sunlight, for instance), specific damage occurs through cycloaddition between the neighboring thymine bases to create a cyclobutyl thymine dimer. Common solar light quanta in the range 250–300 nm evoke formation of the depicted thymine dimers (containing cyclobutane rings) in suitable regions of the duplex DNA. This lesion is potentially very dangerous. Fortunately, these regions in double-stranded DNA with dangerous defects are readily recognized by a number of DNA repair enzymes. A cell possesses various ways to deal with the dimers (to repair this DNA damage). Some cells simply excise the dimers from their DNA strands. Other cells use DNA photolyase enzymes that simply break the cyclobutane structure, restoring the two adjacent, undamaged, thymine units. This requires photoexcitation (330–400 nm) of the enzyme, which then transfers one electron to the dimer, and thus, can repair the dimer by electron reduction (see Schemes 3.71 and 3.72). The resulting anion-radical then breaks open, and the electron is returned to the enzyme.

DNA strands were recently prepared containing a cyclobutane-thymidine dimer lesion and a flavin building block. These doubly modified DNA strands show light-induced self-repairing properties (Schwogler et al. 2000). Flavin acts as an electron donor to the dimer acceptor in this DNA strand. The basis of the repair reaction, which rescues many insects, fish, amphibians, and plants from UV-induced cell death and mutagenesis, is a light-induced electron transfer from a reduced and deprotonated flavin coenzyme to the DNA lesion. Despite the wide occurrence of this repair process in nature, it is not clear whether it is used in the human body or not. This is a highly controversial area at present, with strong views on both sides (Podmore et al. 1994, de Grujil and Roza 1991). What is crucial for our consideration is the rapid breakdown of the dimer following electron addition before an electron can return to the enzyme. A special study of the anion-radical of the thymine dimer revealed that it gives the monomer and the monomer anion-radical rapidly, even at 77 K. Splitting is depicted in Scheme 3.72 (Pezeshk et al. 1996).

An *ab initio* study on the structure and splitting of the uracil dimer anion-radical (see Scheme 3.72, R = H) gives preference to the one-step mechanism (Voityuk and Roesch 1997). Anion-radical anions of the pyrimidine dimers cleave with rate constants in excess of 10^6 s^{-1}



SCHEME 3.72

(Yeh and Falvey 1991). However, the cyclobutyl dimer of a quinone, and a dithymoquinone, also cleaves on single-electron reduction but much slower than the pyrimidine dimers (Robbins and Falvey 1993). It is truly an unresolved issue as to why the anion-radical cleavage depicted in Scheme 3.72 is so facile. Water participation can probably decrease the barrier of the cycloreversion on physiological conditions (Saettel and Wiest 2001, 2006). Besides, hydration effect is known to increase the electron affinities of nucleic bases (Scheidt et al. 1998, Kim and Schaefer 2007a, 2007b).

Oxidative repair of DNA damage is also possible since the radical cation of the thymine cyclobutane dimer is similarly unstable (Kruger and Wille 2001). Employing catalytic rhodium complexes attached to the DNA strands, Dandliker et al. (1997) have shown that the duplex strand can shuttle a positive charge to a damaged site over a distance of at least 2.6 nm. The charge is transferred to the dimer, generating the dimer cation-radical. This cation-radical rearranges back into a normal thymine doublet. After that, the positive charge returns to the rhodium complex. The reparative reaction occurs in sunlight or at 400 nm.

Hence, the DNA duplex is a good medium for electron transfer reactions even over long distances (according to Abdou et al. 2001, over distances greater than 3.0 nm). The concept of DNA as "an electron-conductive wire" works in the case of guanine doublets, too (Arkin et al. 1996). This long-range charge migration can promote a repair of a common photochemical lesion in DNA. Such an opportunity to repair the lesion has opened a new and interesting approach to genetic engineering.

There is another important aspect of DNA damages. A unique feature of many cancerous tumors is the existence of hypoxic regions, that is, regions of oxygen-poor cells (Brown 1999). Such cells are often resistant to more conventional forms of antitumor treatment such as radiotherapy and chemotherapy (Denny and Wilson 2000). There has been considerable effort for the identification

of potential antitumor drugs that specifically target such cells. One such class of potential hypoxia-specific drugs is the benzotriazine *N*,*N*′-dioxides, of which a particularly promising candidate is 3-amino-1,2,4-benzotriazine-1,4-dioxide or tirapazamine (Brown and Wang 1998). Tirapazamine provides DNA cleavage in hypoxic tumor cells. This dioxide undergoes an enzymatic one-electron reduction to form the corresponding anion-radical. Then hydrogen abstraction from DNA takes place, eventually resulting in the killing of cancer cells. The ion-radical hypothesis seems to be promising in the search for new anticancer medications.

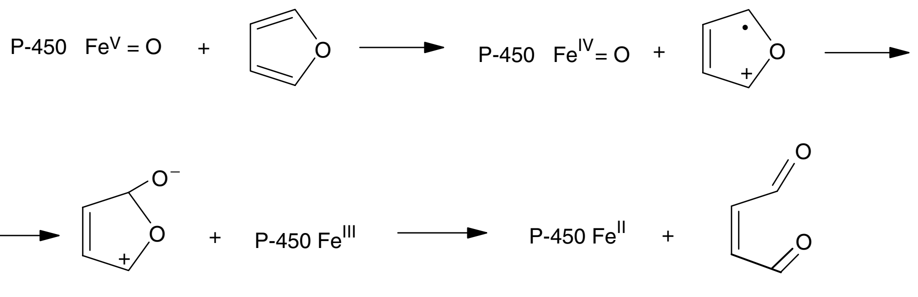
3.4.4 Cation-Radical Intermediates in Metabolism of Furan Xenobiotics

One compound of interest originating from natural sources is 3-methylfuran. This pneumotoxic compound was identified in smog and is believed to arise from photodecomposition of naturally occurring terpenoids (Saunders et al. 1974). As mentioned earlier, cytochrome (P-450)-catalyzed oxidation may proceed by discrete, one-electron steps. When a microsome suspension containing 2- or 3-methylfuran was incubated in the presence of semicarbazone, ene-dialdehyde products (acetylacrolein or 2-methylbutenedial) were isolated as bis(semicarbazones). Ravindranath et al. (1984) have provided (on the basis of solid and diverse proofs) the following sequence of transformations: P-450 $Fe^{V} = O$ gives P-450 $Fe^{IV} = O$ (which possesses a radical character), and furan gives its cation-radical. The latter is stable enough to leave the site of its formation, but too reactive to migrate far. Radical-radical interaction between these two products of one-electron transfer leads to butenedial. This sequence is shown in Scheme 3.73, with unsubstituted furan as a participant of the biological reaction. The final ene-dialdehyde is quite reactive and is the cause of an eventual damage in living organisms.

3.4.5 Behavior of Anion-Radicals in Living Organisms

The majority of the enzyme-catalyzed reactions discussed so far are oxidative ones. However, reductive electron transfer reactions take place as well. Diaphorase, xanteneoxidase, and other enzymes as well as intestinal flora, aquatic, and skin bacteria—all of them can act as electron donors. Another source of an electron is the superoxide ion. It arises after detoxification of xenobiotics, which are involved in the metabolic chain. Under the neutralizing influence of redox proteins, xenobiotics yield anion-radicals. Oxygen, which is inhaled with air, strips unpaired electrons from these anion-radicals and gives the superoxide ions (Mason and Chignell 1982).

Some biologically important *o*-quinones can react with the superoxide ion giving catechol derivatives, which may play a role in many diseases. For example, compounds bearing a nitrocatechol moiety have been claimed to be efficient catechol-*O*-methyl transferase inhibitors (Suzuki et al. 1992, Perez et al. 1992). The transferase is the first enzyme in the metabolism of catecholamine; a hyperactivity of this enzyme leads to Parkinson's disease. Therefore, prediction of biological activity and antioxidant properties of quinones is an important challenge for researchers.



SCHEME 3.73

Smertenko et al. (2000) have proposed a special index for this purpose based on differences in redox potentials between a quinone and oxygen. This index takes into account the peak merging for electrochemical reductions of the quinone and oxygen and, according to first estimations, works well.

Electrochemical reduction of monocyclic endoperoxide showed one important method to study marine metabolite activity (Stringle et al. 2003). Monocyclic endoperoxides are compounds that contain an oxygen–oxygen bond within a cyclic molecular framework. Chondrillin and muqubilin are representative examples of such metabolites, which display antitumor, antimicrobial, and antiviral activities. Stringle et al. (2003) studied the transformation of a model compound, 3,3,6, 6-tetraphenyl-1,2-dioxane. In this case, a single-electron transfer disrupts the oxygen–oxygen cyclic bond. The resulting distonic anion-radical bears an unpaired electron on one of the oxygen atoms and a negative charge on the other. Both the acyclic oxygens are separated with four carbons. This distonic (open-chain) anion-radical eliminates ethylene and generates benzophenone and benzophenone anion-radical. The latter transfers its unpaired electron to the starting dioxane, initiating the chain process. Such a type of reactivity is probably present in the mechanism of the marine metabolite transformation in living organisms.

Biotransformation pathways of nitroaromatic compounds are believed to originate from nitroreductases that have the ability to use nitro aromatics either as one- or two-electron acceptors. One-electron acceptance by the nitro compounds results in the production of the nitro anion-radical. This anion-radical becomes one of the most aggressive species in biological systems because of its reaction on endogenous molecules and well-known catalytic ability to transfer one electron to molecular oxygen, with the formation of the superoxide ion. Thus, activation of nitrofurantoin—the medication against the urethral disease—proceeds by one-electron reduction of the nitro group (Youngman et al. 1982). Nimesulide [*N*-(4-nitro-2-phenoxyphenyl) methanesulfonamide], as one of calcium ion antagonists, forms the anion-radical that is actively scavenged by endobiotics like adenine (Squella et al. 1999). Importantly, in this group of drugs (alongside nifedipine, nimodipine, and nicardipine) the nimesulide nitro anion-radical presents a weaker reactivity than anion-radicals of the other representatives. This could be considered as an advantage in chronic treatment, where the appearance of toxicity is more possible.

The biological oxidant P-450 can also catalyze reduction, cycling between the Fe^{II} and Fe^{III} forms (Guengerich and Macdonald 1993). The preponderance of oxidation reactions is not surprising, because in the sequence of oxygen activation steps, ferrous P-450 binds O_2 rapidly and tightly.

$$\text{P-450 [Fe]}^{III} + e \rightarrow \text{P-450 [Fe]}^{II} + O_2 \rightarrow \text{P-450 [FeO}_2]^{II}$$

As Guengerich and Macdonald (1993) pointed out, P-450 reduction must competitively involve binding of the substrate in a manner that is analogous to that of the molecular oxygen. For the P-450 binding with oxygen, the oxygen-expansive force should be significant. It means that the oxygen pressure must be marked. As for a substrate, it needs to have sufficient redox potential to perform easy reductase-mediated reduction. Although the oxygen-expansive force is sometimes rather low in cells of the liver and other tissues, reductive reactions proceed in some cases. All of the reductions must be one-electron processes similar to Fe^{III}/Fe^{II} couple transition.

Reductive dehalogenation reactions catalyzed by P-450 have been studied extensively, primarily because of the interest in compounds such as anesthetics, pesticides, and potentially toxic industrial solvents. An anesthetic named *halothane* gives anion-radical that undergoes dehalogenation according to the following equation:

$$CF_3\text{–}CHBrCl + e \rightarrow [CF_3\text{–}CHBrCl]^{-\bullet} \rightarrow CF_3\text{–}CH^{\bullet}Cl + Br^-$$

$$CF_3\text{–}CH^{\bullet}Cl \rightarrow CF_2\text{=}CHCl + F^{\bullet}$$

In the preceding equation, the primary anion-radical gives the 1-chloro-2,2,2-trifluoroethyl radical. *In vivo*, this radical was detected by the spin-trapping method (Poyer et al. 1981). Ahr et al. (1982) had presented additional evidence for the formation of the radical as an intermediate in halothane metabolism and identified 1-chloro-2,2-difluoroethene as a product of radical stabilization. Metabolytic transformations of 1-chloro-2,2-difluoroethene lead to acyl halides, which are relevant to halothane biotoxicity (Guengerich and Macdonald 1993).

In the case of tetrachloroethylene and trichloroethylene, reductive dehalogenase of *Sulfurospirillum multivorans* provides access to their dehalogenation giving rise to (Z)-1, 2-dichloroethene with exceptionally high specific activities. The initial electron transfer results in the formation of the polychloroethene anion-radicals; their further degradation is detailed in the review by Costentin et al. (2006). It should be emphasized that common chlorinated solvents, such as polychloroethanes and polychloromethanes, form one of the main groups of environmental pollutants present in the soil and underground waters of many industrial sites. This contamination is especially dangerous in view of their toxicity or carcinogenic nature. The metabolism of carbon tetrachloride (a chemical solvent that was formerly in common use) attracts attention as well. Its bioactivation appears to involve consecutive one-electron reduction and the formation of chloride ion with the trichloromethyl radical. The latter radical then reacts with oxygen, giving rise to an oxygenated radical and, eventually, a high toxic phosgene (Mico and Pohl 1983):

$$CCl_4 + e \rightarrow [CCl_4]^{-\bullet} \rightarrow {}^{\bullet}CCl_3 + Cl^-$$

$${}^{\bullet}CCl_3 + O_2 \rightarrow CCl_3OO^{\bullet} \rightarrow COCl_2$$

Probably, the spontaneous degradation of methyl bromide in the oceans reported by Butler (1997) has a similar mechanism. Both nature and humans contribute to the world's production of methyl bromide. This compound is thought to be responsible for a significant fraction of the ozone-destroying bromine that reaches the stratosphere. Compared to the results of the chemical degradation in the oceans, the danger of methyl bromide in the higher layers of the atmosphere is not so significant. Researches from the National Oceanic and Atmospheric Administration (United States) reported that previously unrecognized biological degradation of atmospheric methyl bromide proceeds in the same extent as oxidation with ozone participation. Nevertheless, methyl bromide is still used widely to limit the spread of the damaging insect population around the world.

For example, the lack of good alternatives pushed the U.S. Department of Agriculture in 1998 to recommend the use of methyl bromide to treat wood packaging materials from China. A voracious, nonnative insect pest had been found in such packaging materials in 14 states around the United States. The Asian beetle had no known U.S. predators and could cost the United States more than $41 billion in lost forest product, commercial fruit, maple syrup, nursery, and tourist industries. This beetle was an extremely serious insect, and methyl bromide was the only known effective insecticide. Heat treatment was also suggested, but it proved to be more difficult and expensive (Morse 1998). Therefore, methyl bromide as an insecticide was receiving a reprieve.

3.5 CONCLUSION

This chapter set out approaches for binding electron structures of organic ion-radicals with their reactivity. Of course, an amount of structural data is much greater than the data on reactivity. It is commonplace in this field that structural (instrumental) data are accumulated more rapidly than data on reactivity from chemical experiments.

The systematization provided here is useful for the future development of ion-radical organic chemistry. (Systematization is fruitful for every field of science.) It is worthwhile to underline several aspects of the considered materials that can enhance their possible applications.

Research on spin–charge separation in distonic ion-radicals has been carried out in recent years with an emphasis on theoretical calculations. Experiments were performed to prove their existence and observe their behavior in a mass spectrometer chamber. The next step is likely to emphasize the synthesis of the distonic ion-radical salts, which could be stable under common conditions. Applications of the salts would be possible in creating magnetic, conductible media and other materials possess practically useful properties. The attractive strength of distonic ion-radicals is that they can enter ionic reactions at the charged site and radical reactions at the radical site. Success in this direction can open a new window in terms of organic reactivity.

Understanding ion-radical transformations in living organisms is also very important. The problem is intriguing in general. Our aim is to make some incentives for overcoming ecological obstacles and designing new and effective medications.

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4 Discerning Mechanism of Ion-Radical Organic Reactions

4.1 INTRODUCTION

A reaction mechanism is the sum of the perceived elementary stages taken in their sequence and relative rate. A knowledge of the properties of intermediate particles and study of the mechanism of reactions open up possibilities of increasing the rate of formation and yield of the desired final product. Transformations, including the formation of ion-radicals in the intermediate step, require special approaches to optimize them. In other words, it is necessary to determine whether the reaction proceeds through the formation of ion-radicals and, if so, which particles originate and at what stages. It is essential to learn whether these stages belong to the main or side routes of the reactions.

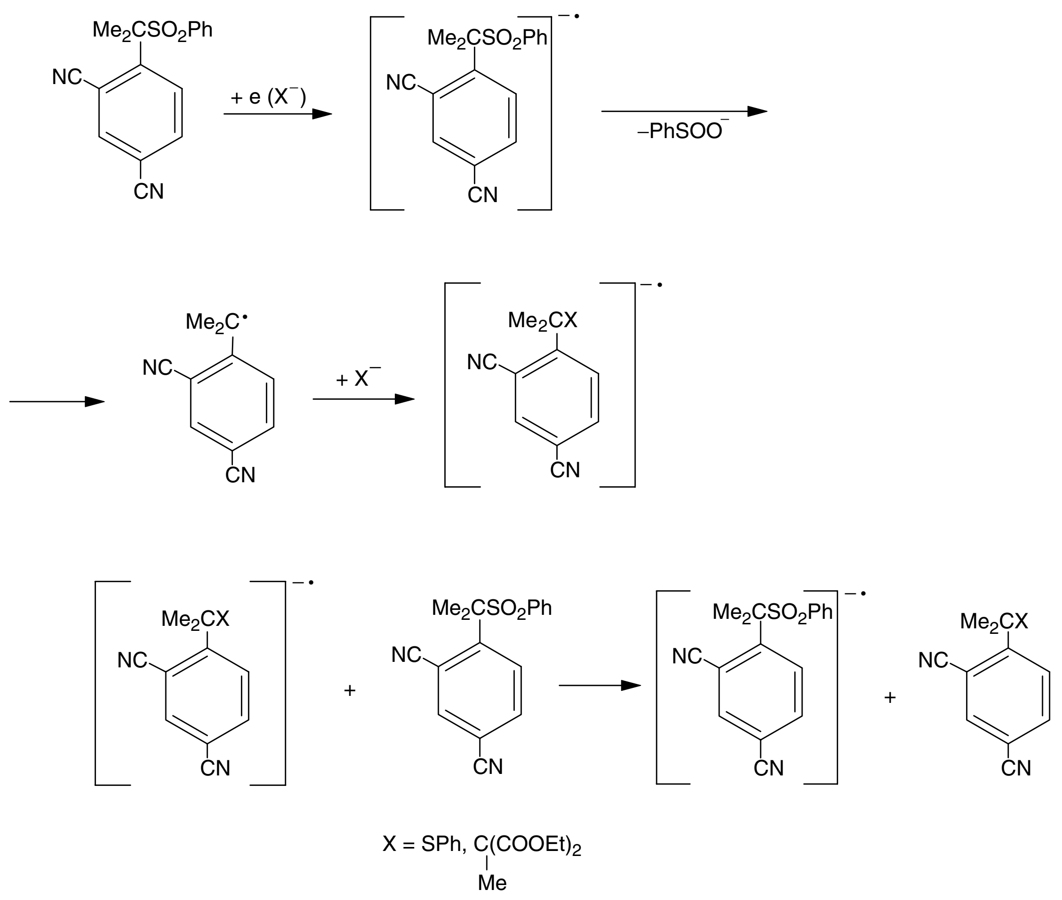
This chapter just devotes to such problems. This chapter describes how one can reveal ion-radical conversions by means of physical methods and kinetic approaches and on purely chemical information, including data on material balance and the nature of end products. These methods are woven together to form a cohesive unit. All the methods are considered separately, and then complex approaches are described in their applications to several representative reactions.

4.2 WHY DO REACTIONS CHOOSE ION-RADICAL MECHANISM?

The functional groups in a molecule determine, to a considerable extent, whether its ion-radical form is the leading particle in the course of the reaction. The effect of substituents on the properties of the ion-radical molecule has not been elucidated adequately. The main problem is to find out what groups should be introduced into the molecule to direct the reaction to ion-radical mechanism. At first, these groups should impart pronounced acceptor or donor properties to the molecule. Then, these groups must stabilize the ion-radical produced. As to anion-radicals, such groups are nitro, cyano, carbonyl and sulphonyl, and trifluoromethyl (when more than one CF_3 group are present in the molecule). This list, however, is not final; it will be completed as the research yields new data. As to cation-radicals, such strong donors as the methyl and amino groups are considered stabilizers for cation-radicals. Cation-radicals are more reactive than anion-radicals, and the cation-radical center must be shielded. Therefore, scientists prefer to use donor substituents loaded with different fragments such as the *N*,*N*-dialkylamino group or vinyl group carrying alkyl substituents. The following examples illustrate these regularities.

The reaction of *o*,*p*-dicyano-α-phenylsulphonyl cumene with sodium thiophenolate in DMF produces *o*,*p*-dicyano-α-phenylthiocumene. A product of similar substitution is obtained with the potassium salt of diethyl malonate as a reactant (Kornblum and Fifolt 1980; Scheme 4.1).

Irradiation accelerates the reactions of Scheme 4.1, and the substitution products are formed in 70–80% yields. Acceptors of radicals (e.g., di-*tert*-butylnitroxyl) or electrons (e.g., *m*-dinitrobenzene [DNB]) completely inhibit the substitution even if the acceptors are added to the reaction mixture in small amounts. The mentioned substitution reactions do not take place when no cyano groups are present in the initial α-phenylsulphonyl cumene. Hence, the cyano groups send the reaction via the ion-radical pathway. Like the nitro group, the cyano group promotes the formation of anion-radical, which originates on one-electron transfer from the thiophenolate or malonate ions to the substrate.



SCHEME 4.1

Of course, the very direction of the anion-radical disintegration depends on substituents. Let us compare the anion-radicals from *p*-cyano-α-nitrocumene and *p*-nitro-α-nitrocumene. As it was established by electrochemical study (Zheng et al. 1999), there is a subtle but important difference in their cleavage. In *p*-cyano-α-nitrocumene case, the charge is located mainly on the α-nitro group. This charge remains there when the cleavage has completed. Nitrite and cumyl radical are formed. In *p*-nitro-α-nitrocumene case, the charge and unpaired electron are originally located in the nitrophenyl portion of the anion-radical, but the charge moves to the leaving nitrite ion. The spin density (an unpaired electron) remains within the nitrophenyl group.

Now, a substrate molecule should carry groups that can promote the formation and stabilize the ion-radical produced. For a reactant molecule, it should lose or trap an electron, otherwise the substrate will not form an anion- or cation-radical. A radical produced from an ion-radical after the separation of a leaving group should possess certain elecrophilicity and nucleophilicity with respect to anion and cation reactants, respectively. For example, radicals bearing electron-acceptor groups should add negatively charged reactants more easily than radicals devoid of such groups. For a chain process to develop, the molecule of the initial substrate should enter into electron transfer more readily (be more of an acceptor or a donor) than the product molecule. Only in this way, the unpaired electron density can move from the product ion-radical to the initial uncharged substrate (this requirement will be detailed in Section 4.5.3). And finally, the reactant should effectively capture radicals formed from the substrate. The remaining chapters detail these requirements in a series of examples.

In a range of anions PhZ^- (Z = O, S, Se, Te), for example, the thiophenolate ion (PhS^-) effectively traps aryl radicals ($Ar^\bullet$), whereas the anion of phenyl selenide ($PhSe^-$) is 20 times less active, and the phenolate anion (PhO^-) is absolutely inactive. The reaction of aryl radicals with phenyltelluride ions ($PhTe^-$) proceeds in an abnormal fashion—both asymmetrical and symmetrical tellurides are produced (Rossi and Pierini 1980).

$$Ar^\bullet + PhTe^- \rightarrow Ph_2Te + ArTePh + Ar_2Te$$

As MO calculations show (Vilar et al. 1982), the energy levels for pairs ($Ar^\bullet + {}^-TePh$) and ($ArTe^- + Ph^\bullet$) are equal. This makes a dual direction of decomposition possible for the intermediate anion-radical as follows:

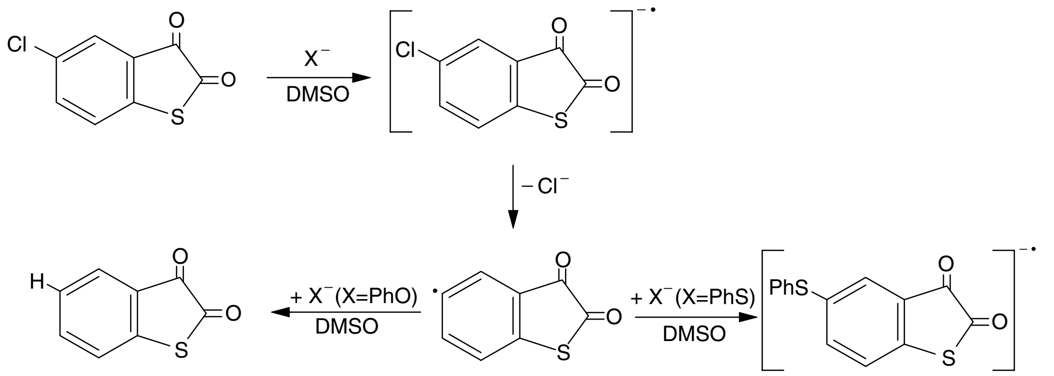
$$Ar^\bullet + {}^-TePh \leftarrow (Ar^\bullet\,{}^-TePh \leftrightarrow ArTe^{-\bullet}Ph) \rightarrow ArTe^- + {}^\bullet Ph$$

Many reactions demonstrate a high activity of the phenylthiolate ion in trapping aryl radicals and inability of the phenolate ion to do so. Thus, the phenylthiolate ion acting on 5-chloro-2*H*,3*H*-benzo[b]thiophenedione-2,3 produces the substitution product (in anion-radical form), whereas the phenolate ion initiates only the reductive dechlorination (Ciminale et al. 1978; Scheme 4.2).

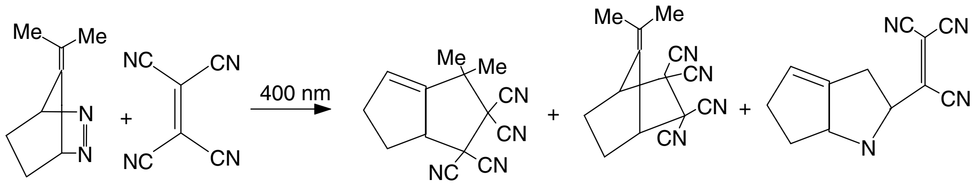
To disrupt the carbon–chloride bond at position 5 of the substrate anion-radical, population of this bond with an unpaired electron should be increased. However, if a spin density at carbon-carrying chlorine is too great, the initial chlorine-containing anion-radicals dimerize instead of cleaving the chloride ion. Thus, in the isomeric 6-chloro-2*H*,3*H*-benzo[b]thiophenedione-2,3 anion-radical, unpaired electron density at C-6 is five times greater than at C-5, and the dimerization proceeds much more rapidly than the cleavage of carbon–chlorine bond (Alberti et al. 1981).

The dissociation energy of the bond being broken is an additional crucial factor for ion-radical pathway. In a series of α-halosubstituted acetophenones, for instance, the fluoro substituent provides an out-of-row example of anion-radical cleavage reactivity. This is a general rule—aromatic fluorine-containing anion-radicals do not readily dissociate into aryl radicals and fluoride ions (Denney et al. 1997). The strength of carbon–fluorine bond significantly contributes to slowing down the cleavage, as opposed to other substituents in all of the reactions where solvent reorganization is largely predominant (Andrieux et al. 1997).

A solvent role can play a decisive role when a reaction chooses the ion-radical pathway. Thus, the solvent effect on thermodynamic contribution to activation free energy causes an increase in the



SCHEME 4.2



SCHEME 4.3

cleavage rate constant for chloroanthracene anion-radical with an increase of the solvent acceptor number. There are examples of similar solvent effects in a review by Jaworski (1998).

Sometimes, researchers are changing solvent polarity deliberately, to discern the origin of reaction products. A representative case is the photoreaction depicted in Scheme 4.3; the reaction gives rise to the following three products.

The yields of the first two products are insensitive to changes in solvent polarities. The yield of the third (the last) product increases with changing the solvent from CD_2Cl_2 to CD_3CN and, especially, addition of $LiClO_4$ to CD_3CN reaction medium. Obviously, the third product is formed on a parallel reaction having ion-radical mechanism (for details, see Painter and Blackstock 1995). The dependence of reaction kinetics on ionic strength can supposedly be an indicator of ion-radical participation in rate control.

Attractive interactions between ion-radicals and their environment may lower the energy of the corresponding MO populated with an unpaired electron. This enhances the stability of ion-radicals and favors the stepwise pathway of the reaction; for example, $RX + e \rightarrow (RX)^{-\bullet} \rightarrow R^{\bullet} + X^{-}$. Contrary to the stepwise mechanism, a concerted mechanism of dissociate electron transfer is also possible, for example, $RX + e \rightarrow R^{\bullet} + X^{-}$. The competition between these two reaction pathways depends on both the driving forces and intrinsic barrier factors. As proved for several anion-radical reactions, there is a rule for a reaction to proceed down the stepwise or concerted mechanism. The higher the energy of the lowest unoccupied MO and weaker the bond strength between R and X in the starting molecule, the greater is the tendency for the concerted mechanism to prevail over the stepwise mechanism, and vice versa (Andrieux et al. 1994).

Thus, if the concerted pathway has a stronger driving force than that of the first step of the stepwise pathway, the cleavage of anion-radical is thermodynamically favorable. Stepwise mechanisms are considered viable when the intermediate (anion-radical in the preceding schemes) has a lifetime that is longer than the time for a bond vibration (ca. 10^{-13} s). Concerted mechanisms occur under opposite conditions, that is, when the intermediate does not exist (Eldin and Jencks 1995, Speiser 1996). However, another point of view has developed according to which the concerted character of a reaction results from an energetic advantage rather than from the nonexistence of the ion-radical intermediate (see, e.g., Andrieux et al. 1997).

Considering energy factors that govern the reaction pathway, it is worthwhile noting the mode of electron injection (abstraction). For instance, the energy of the incoming electron is much larger in pulse radiolysis than in electrochemistry. The additional driving force thus offered can stimulate a transition from a concerted to a stepwise mechanism (Andrieux et al. 1995).

As to the further fate of the formed radical $R^{\bullet}$, it may be trapped with the reactant ion, say Z^{-}, and transformed into $(RZ)^{-\bullet}$ anion-radical. The latter will pass an unpaired electron to RX to start a new reaction sequence. Therefore, the starting compound must have a greater electron affinity than the substitution product. This is necessary to develop the described chain process. Another pathway to stabilize the radical $R^{\bullet}$ is its dimerization–$R^{\bullet} + R^{\bullet} \rightarrow R$–$R$.

This route leads to termination of the chain process. Large concentrations of the substrate and small concentration of the nucleophile are the factors favorable for the formation of the dimer. This statement concerns only the reaction in which the attack of the nucleophile on the radical $R^{\bullet}$ proceeds in a moderate rate (Ettaeb et al. 1992).

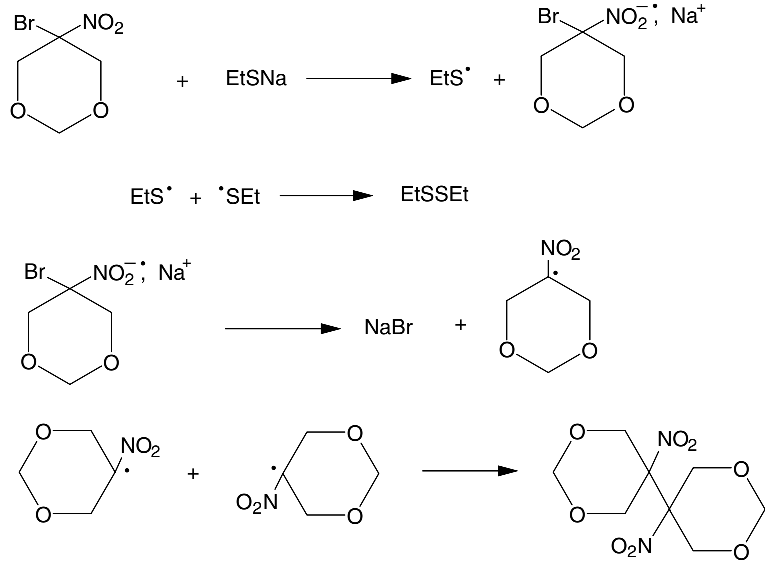
4.3 CHEMICAL APPROACHES TO IDENTIFICATION OF ION-RADICAL ORGANIC REACTIONS

4.3.1 Identification According to Structure of Final Products

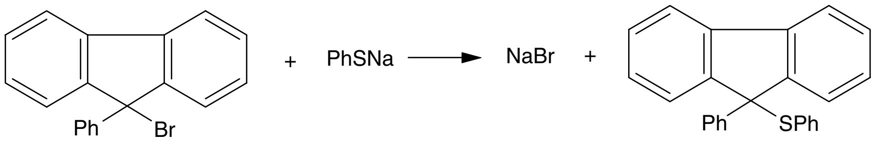
The interaction of alkyl halides with mercaptans or alkaline mercaptides produces thioalkyl derivatives. This is a typical nucleophilic substitution reaction, and one cannot tell by the nature of products whether or not it proceeds through the ion-radical stage. However, the version of the reaction between 5-bromo-5-nitro-1,3-dioxan and sodium ethylmercaptide can be explained only by the intermediate stage involving electron transfer. As found (Zorin et al. 1983), this reaction in DMSO leads to diethyldisulfide (yield 95%), sodium bromide (quantitative yield), and 5,5′-bis(5-nitro-1,3-dioxanyl) (yield 90%). UV irradiation markedly accelerates this reaction, whereas benzene nitro derivatives decelerate it. The result obtained shows that the process begins with the formation of ethylthiyl radicals and anion-radical of the substrate. Ethylthiyl radicals dimerize (diethyldisulfide is obtained), and anion-radicals of the substrate decompose monomolecularly to give 5-nitro-1,3-dioxa-5-cyclohexyl radicals. The latter radicals recombine and form the final dioxanyl (Scheme 4.4).

Another representative and important example is the thioarylation of 9-bromo-9-phenylfluorene. The reaction yields sodium bromide and 9-phenylthio-9-phenylfluorene (Singh and Jayaraman 1974; Scheme 4.5).

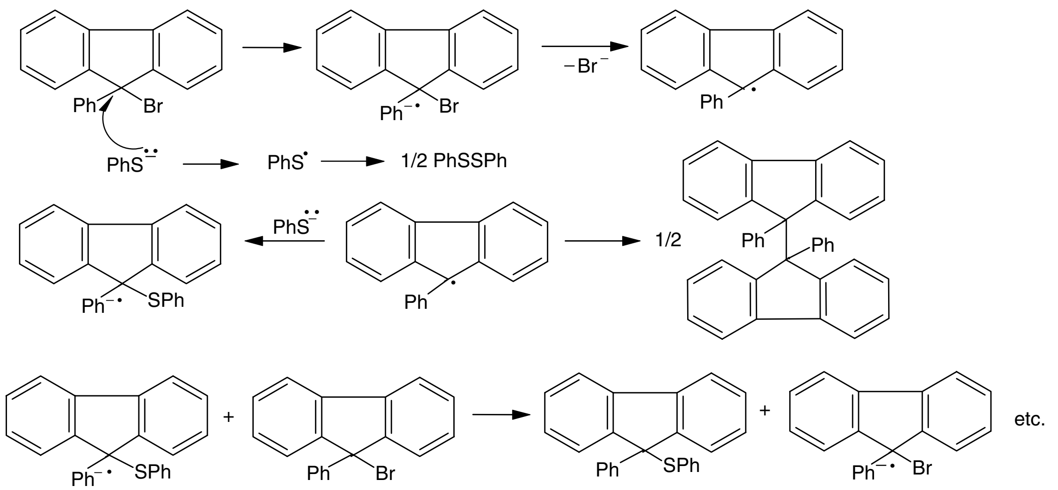
In this reaction, sodium bromide is produced in the quantitative yield, but the yield of the product of nucleophilic substitution is only 42%. The substrate and nucleophile also enter into other conversions leading to 9,9′-diphenylbifluorenyl (yield 33%) and diphenyldisulfide (yield 30%).



SCHEME 4.4



SCHEME 4.5



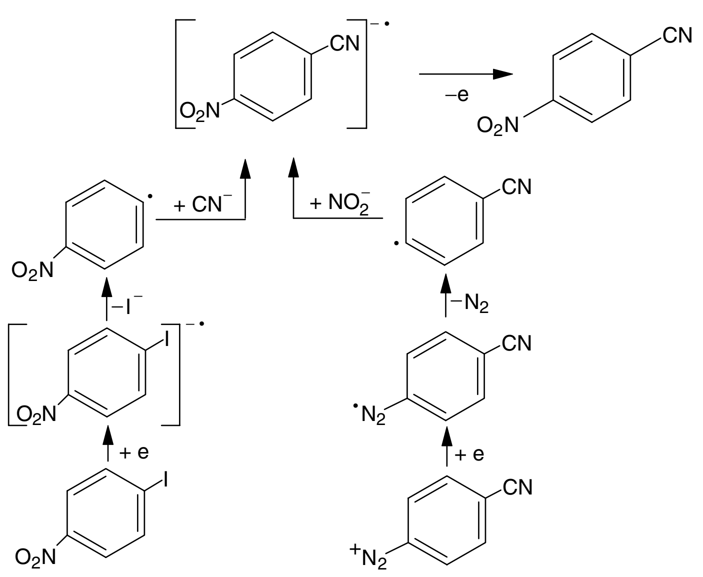
SCHEME 4.6

The formation of these substances contradicts common ideas on nucleophilic substitution. The presence of radical traps (oxygen or tetrabromobenzoquinone) decelerates the formation of both unexpected compounds and product of thioarylation. Consequently, the first stage of the reaction depicted in Scheme 4.5 produces phenylthiyl radical and anion-radical of the substrate. Both electron-transfer products undergo further conversions: The phenylthiyl radical gives diphenyldisulfide, and the anion-radical of the substrate produces 9-fluorenyl radical. The latter reacts in two directions—dimerizing, it forms bifluorenyl; reacting with the nucleophile, it gives the anion-radical of the substitution product. The chain continues because the electron from the anion-radical is transferred to the unreacted molecule of the substrate. The latter loses bromine and then reacts with the nucleophile, and so on (Scheme 4.6).

The mechanism of the reaction depicted in Scheme 4.6 differs from the S_N1 or S_N2 mechanism in that it involves the stage of one-electron oxidation–reduction. The impetus of this stage may be the easy detachment of the bromine anion followed by the formation of fluorenyl radical. The latter is unsaturated at position 9 near three benzene rings that stabilize the radical center. The radical formed is intercepted by the phenylthiolate ion. This leads to the anion-radical of the substitution product. Further electron exchange produces the substrate anion-radical and final product in its neutral state. The reaction consists of radical (R)-nucleophilic (N) monomolecular (1) substitution (S), with the combined symbol $S_{RN}1$. Reactions of $S_{RN}1$ type can have both branch-chain and nonchain characters.

The chain mechanism is, apparently, more common than nonchain one. The very conception of $S_{RN}1$ reaction was formulated as a result of chain-radical theory development. In 1964, alkylation of a saturated carbon atom bearing a good leaving group was found to be proceeding through one-electron transfer, resulting in the formation of anion-radicals and radicals. Kornblum and his colleagues were the first ones to discover such a mechanism (Kerber et al. 1964, 1965). Kornblum et al. (1966) as well as Russell and Danen (1966) had independently shown that such substitution develops as the chain process. As found later, the chain-radical mechanism, with anion-radical participation, takes place in some cases of aromatic nucleophilic substitution and subsequently the symbol $S_{RN}1$ was proposed (Kim and Bunnett 1970).

The $S_{RN}1$ mechanism has been proven via many different approaches. Russell et al. (1971) reconstructed the stage of nucleophilic substitution of 4-iodonitrobenze with cyanide ion according to Scheme 4.7.



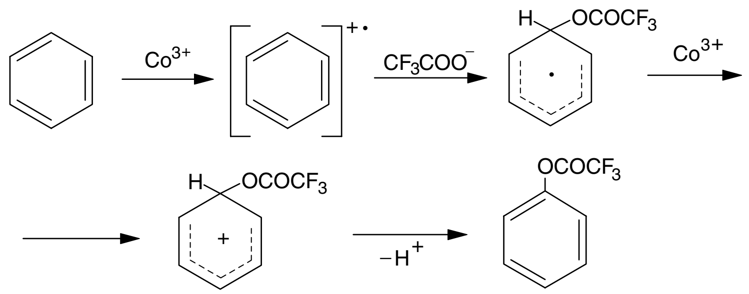
SCHEME 4.7

One-electron reduction at the cathode in the presence of cyanide leads to anion-radical of 4-iodonitrobenzene. Like other halide derivatives, 4-iodonitrobenzene in the anion-radical state easily expels the halide ion and converts into 4-nitrophenyl radical. The latter reacts with cyanide ion and produces anion-radical of 4-cyanonitrobenzene. The same anion-radical can be obtained by reducing the 4-cyanobenzenediazonium salt with dithionite in the presence of nitrite. One-electron oxidation with the initial substrate converts this anion-radical into 4-cyanonitrobenzene.

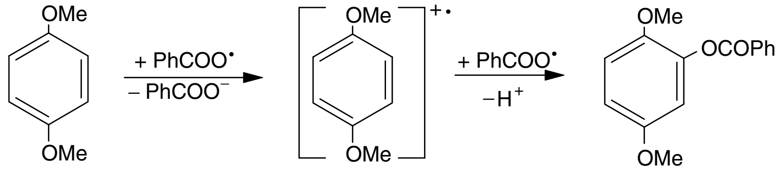
Principally the same, but chemically simpler, sequence was used to prepare arylnitro anion-radicals from arylamines, in high yields. For instance, aqueous sodium nitrite solution was added to a mixture of ascorbic acid and sodium 3,5-dibromo-4-aminobenzenesulfonate in water. After addition of aqueous sodium hydroxide solution, the cation-radical of sodium 3,5-dibromo-4-nitrobenzenesulfonate was formed in the solution. The latter was completely characterized by its ESR spectrum. Double functions of the nitrite and ascorbic acid in the reaction should be underlined. Nitrite takes part in diazotization of the starting amine and trapping of the phenyl σ-radical formed after one-electron reduction of the intermediary diazo compound. Ascorbic acid produces acidity to the reaction solution (needed for diazotization) and plays the role of a reductant when the medium becomes alkaline. The method described was proposed for ESR analytical determination of nitrite ions in water solutions (Lagercrantz 1998).

The acetoxylation of aromatic compounds, chemically or at the anode, produces similar results. Kochi et al. (1973) found a way of stabilizing aromatic cation-radicals in trifluoroacetic acid. The method involves rapid mixing of the solutions of aromatic compound and trifluoroacetates of trivalent cobalt and freezing the mixture. During thawing, the samples give well-resolved ESR spectra of aromatic cation-radicals. The latter convert into aryl esters of trifluoroacetic acid. One molecule of the aromatic compound consumes two molecules of the oxidizer; the limiting stage of the reactions is one-electron oxidation producing the cation-radical (Scheme 4.8).

The anode acetoxylation of aromatic compounds in solutions of acetic acid carrying alkali or tetraalkylammonium acetates takes the same route. As shown (Eberson 1967, Eberson and Jonsson 1981), the process starts with one-electron oxidation at the anode and then passes through the same stages as in oxidation with cobalt trifluoroacetate. The reaction takes place at potentials sufficient to oxidize the substrate but not sufficient to convert acetate ion into acetoxy radical.



SCHEME 4.8



SCHEME 4.9

Interestingly, the acetoxyl group in the product comes not from acetic acid (a solvent) but from acetate ion (a conducting electrolyte)—salts with tosylate or perchlorate anions stop acetoxylation in the solution of acetic acid.

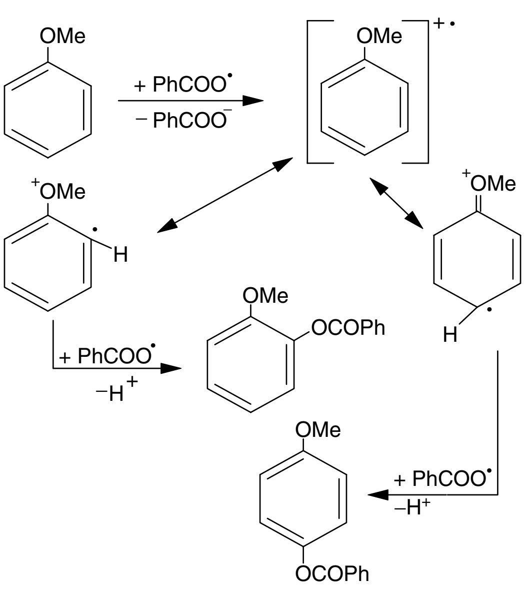
Radical substitution can also proceed through the cation-radical stage. The monograph by Nonhebel and Walton (1974) discusses the introduction of benzoyloxy group into an aromatic ring. Thus, the interaction of benzoyl peroxide with benzene derivatives bearing electron-donor substituents yields the products of hydrogen replacement by benzoyloxyl group. When the ring carries the electron-acceptor substituents, diaryls are formed; in other words, only phenylation takes place. This can be explained with electron transfer from the aromatic substrate to the benzoyloxy radical according to Scheme 4.9.

As evident from Scheme 4.9, one-electron oxidation of 1,4-dimethoxybenzene produces cation-radical. The cation-radical, being more active than the initial substrate, recombines with benzoyloxy radical before the latter decomposes into phenyl radical and carbon dioxide. The process ends in the formation of a stable substitution product.

In case of anisole, the reaction takes the route of Scheme 4.10.

The reaction of Scheme 4.10 yields only products of ortho and para substitutions; the meta isomer is lacking. If it were a standard radical substitution, the meta-isomer would obviously be formed in a certain amount (i.e., in the same amount as that for ortho-substituted product). Introduction of electron-acceptor substituents enhances stability of the substrate to oxidation and prevents electron transfer to benzoyloxy radical. As a result, phenylation takes place instead of benzoyloxylation, and the phenyl radical enters into any free position.

Hence, analyzing the structure of the final products, we can tell whether the reaction has chosen the ion-radical mechanism. To this end, not only the main reaction products but also side or secondary ones should be subjected to analysis. The reaction, however, may yield a single product only. And though the reaction may take the ion-radical pathway, the final product may not differ from the product anticipated from the ordinary reaction. Fortunately, there are also other ways to discern the ion-radical mechanism if the reaction has really chosen it.



SCHEME 4.10

4.3.2 Identification According to Correlation within Reaction Series

Violation of Hammett-type correlation of reaction kinetic constants is a serious indication that the reaction passes from "classical" to ion-radical mechanism. The other name of this type of correlation is σ, ρ analysis according to its mathematical expression $\log k = \log k_0 \pm \rho\sigma$. In this expression, σ is a substituent constant, k_0 the rate constant of an unsubstituted substrate, k the rate constant of a substrate with a substituent, and ρ a slope of the line connecting the substituent constants (σs) and reaction rates (*k*s). For correctness, σ, ρ analysis must operate the rate constants obtained at the experimental temperature, which is far from the isokinetic temperature. Generally, the linear free energy–structure relationship works in cases when thermodynamic contribution to the activation barrier of the given reaction is strongly dependent on the substituent nature. If the linear correlation is disturbed, or if ρ changes, it means that the reaction takes another route. In other words, the compounds begin to react via another mechanism. Various causes can produce changes in the mechanism; however, the move from the classical to the ion-radical route has special manifestations. In ion-radical reactions, the initial step consists of interaction between a donor and an acceptor. This provides us with an additional criterion, namely, the slope of the correlation line (i.e., the sign of the ρ values) obtained for the series of donor substrates and acceptor reactants, separately. In the case of cation-radical mechanism, the substrate series must be characterized with a negative ρ value. This will indicate that a positive charge is developed on the reaction center of the parent donor. Accordingly, a positive ρ value for the reactant series will testify for the negative charge appearance at the reaction center of the parent acceptor, that is, for the anion-radical mechanism.

To get support for the postulation of ion-radical nature of the rate-determining step, one can plot the reaction rate constant values against the oxidation and reduction potentials of the reaction partners. When both plots occur to be linear, it will support the postulation of the ion-radical route.

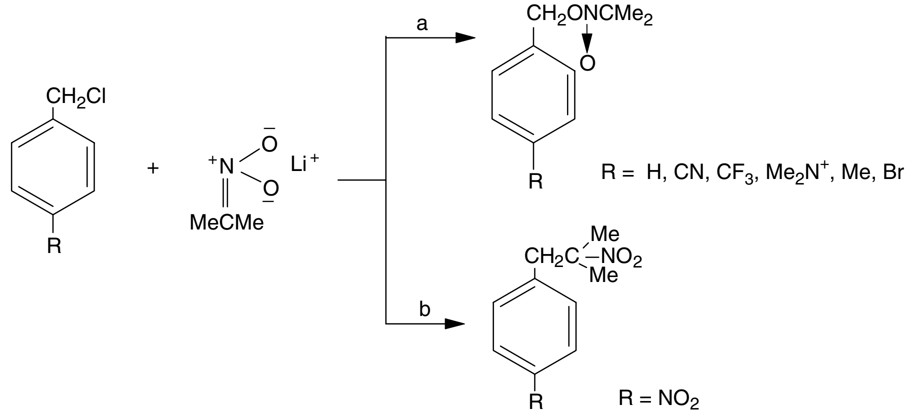
Another common approach consists of the comparison between the experimental rate constants and theoretical values calculated by the procedure developed by Marcus (1956), Marcus and Sutin (1985) as well as Hush (1958). This classical procedure is used widely. Premsingh et al. (2004) gave the relevant references and described a detailed procedure to analyze the ion-radical reaction between anilines and chromium (V) complexes of azomethyne derivatives. Lepage et al. (2003) studied transformation of para-substituted thioanisoles to corresponding methylarylsulfoxides

using the chromium–azomethyne complex as an oxidant. Hammett analysis was applied to the rates of this oxidation. Although direct polar conjugation does exist between a substituent and the reaction center in all of the substrates, correlation to σ constants was not good. Using σ^+ constants, the authors achieved much better correlation. This was qualified as evidence of cation-radical formation at the initial stage. The authors adduced other arguments for one-electron oxidation, but it is sufficient to underline here that the type of reaction constants leading to the best correlation is useful in deciding the ion-radical nature of a reaction.

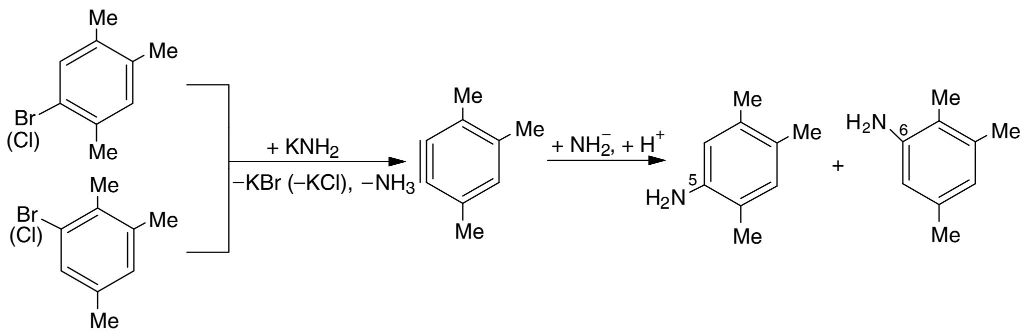
Sometimes, transition from classical to ion-radical mechanism can be established merely according to changes in the character of a product obtained from a definite initial compound belonging to the reaction series under investigation. Thus, interaction of the anion of 2-nitropropane with benzyl chloride and its derivatives bearing the groups CN, CF_3, Me_2N^+, Me, and Br in the para position yields products of O-alkylation (route a in Scheme 4.11). When the substrates contain a nitro group in para position, the reaction leads to the product of C-alkylation (route b in Scheme 4.11). With a nitro group, anion-radicals are more easily produced, occur to be more stable, and the reaction takes the ion-radical pathway (Haas and Bender 1949a, 1949b).

In a similar way, Kim and Bunnett (1970) demonstrated that the substitution of amino group for iodine in iodotrimethylbenzene proceeds via the ion-radical mechanism, in contrast to the bromo and chloro analogs. The reaction of 5- and 6-halo-1,2,4-trimethylbenzenes with potassium amide in liquid ammonia gives rise to 5- and 6-aminoderivatives. This is the cine-substitution reaction (see Scheme 4.12).

As seen, the reaction yields both isomeric amines regardless of the halide position (5 or 6) in the initial molecule. In cases of chloro and bromo analogs, the ratio of 5- and 6-amino derivatives is



SCHEME 4.11



SCHEME 4.12

irrespective of the halide nature and always close to 1.5. The reactions with chloro and bromo analogs proceed according to the same mechanism. For the analogs bearing iodine, this 1.5 ratio decreases to 0.63 in the case of 5-iodo derivative as a starting material and rises to 5.86 in the case of 6-iodo isomer. This means that the iodo derivatives react not only via the mechanism of cine-substitution but also via some other mechanism, the contribution of which differs for 5- and 6-isomers. The iodo derivatives, however, produce the amino derivatives in 1.5 ratio if their reactions are conducted in the presence of *tert*-butylnitroxide or tetraphenylhydrazine. Because these agents scavenge radicals, Kim and Bunnett (1970) concluded that the iodo derivatives react via the mechanism of cine-substitution and at the same time via the ion-radical mechanism. Ion-radicals of iodotrimethylbenzenes cleave the halide ion more readily than bromo and chloro analogs. This coincident route is as follows:

$$ArI \rightarrow [ArI]^{-\bullet} \rightarrow Ar^{\bullet} + I^{-}, \text{ then } Ar^{\bullet} + NH_2^{-} \rightarrow [ArNH_2]^{-\bullet} \quad \text{and}$$

$$[ArNH_2]^{-\bullet} + ArI \rightarrow ArNH_2 + [ArI]^{-\bullet}, \text{ etc.}$$

Let us now consider the formation of aryl iodides from aryl diazonium salts and potassium iodide in methanol (Singh and Kumar 1972a, 1972b). Electron-donor substituents decelerate the process as compared with benzene diazonium (the substituent is hydrogen), whereas electron acceptor substituents accelerate it. Oxygen inhibits the reaction, and photoirradiation speeds it up. As the authors pointed out, in the case of 4-nitrobenzene diazonium, the reaction leads not only to 4-iodonitrobenzene but also to nitrobenzene, elemental iodine, and formaldehyde. All of these facts support the following sequence of events:

$$ArN_2^{+} + I^{-} \rightarrow ArN_2^{\bullet} + I^{\bullet}, I^{\bullet} + {}^{\bullet}I \rightarrow I_2, ArN_2^{\bullet} \rightarrow N_2 + Ar^{\bullet},$$

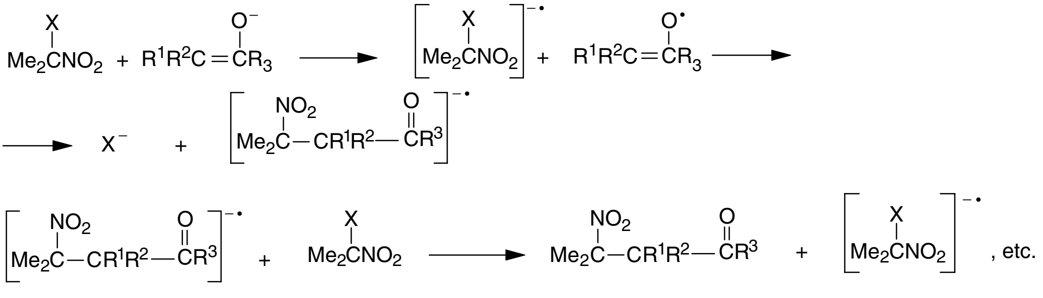
$$Ar^{\bullet} + I^{-} \rightarrow [ArI]^{-\bullet}, [ArI]^{-\bullet} + ArN_2^{+} \rightarrow ArI + ArN_2^{\bullet}, \text{etc.}$$

The nitrophenyl radical can react with the iodide ion and solvent, methanol, as well. Transference of hydrogen radical from methyl alcohol to nitrophenyl radical gives rise to nitrobenzene and formaldehyde ($CH_3OH \rightarrow CH_2O$). Though carefully sought among the products of the reaction, 3-iodonitrobenzene and 4-nitroanisole were lacking. This completely rejects another possible mechanism of the reaction, cine-substitution, which involves the formation of dehydrobenzene as described earlier.

4.3.3 Identification According to Disturbance of "Leaving-Group Strength" Correlation

Classical (standard) nucleophilic substitutions show a clear-cut dependence of process kinetics on the strength of leaving groups. In literature, the leaving group with its electron pair is sometimes called nucleofuge (from composition of Latin words *nucleus* and *fugio*, meaning I am running away). Inclination of the nucleofuge to cleave is called nucleofugicity.

For instance, piperidine replaces a substituent in a series of 4-substituted nitrobenzenes with the following relative rates (DMSO, at 50°C): 1 (Cl), 412 (F), 1.17 (Br), 0.26 (I), and 0.01 (SPh) (Suhr 1964). Similar reactions of amination proceed in liquid ammonia at photostimulation, but the sequence mentioned is disturbed. Bunnett (1978) supported the ion-radical mechanism of the reaction and showed that at the same dose of irradiation, iodides appear to be more active than bromides, whereas chlorides and fluorides react with great difficulty, if at all. Bunnett and Creary (1974a, 1974b) studied the photostimulated reaction of aryl halides as substrates with sodium thiophenolate instead of piperidine as a reagent (liquid ammonia, at −45°C). As shown, aryl iodides undergo substitution, aryl chlorides probably do not react, and aryl bromides are represented by only one example of successful substitution with a yield of arylphenylsulfide of approximately 20%. It is of interest that triethylamine and tetrabutylammonium hydroxide facilitate substitution and PhSNa produces diphenyl disulfide when acting both on bromobenzene (yield 65–70%)



SCHEME 4.13

and chlorobenzene (yield 30–33%) (Rybakova et al. 1982). These bases (triethylamine and tetrabutylammonium hydroxide) act as catalysts. The catalysts probably act as additional electron donors and initiate the formation of the primary anion-radical of the substrate. The anion-radical can originate from the donor–acceptor complex between the substrate and base. This should also promote the decomposition of the anion-radical under photoirradiation.

We see that the disturbance of correlation between the ease of the reaction and strength of a leaving group definitely supports the ion-radical mechanism. This, however, cannot be a sufficient proof because, as pointed out earlier, cine-substitution through arynes also disturbs a common correlation. Besides, the nature of X affects only the rate of fragmentation $ArX^{-\bullet} \rightarrow Ar^{\bullet} + X^{-}$. Indeed, the rate of fragmentation of anion-radicals increases in the series F, Cl, Br, I (Tremelling and Bunnett 1980). If we pump a strong energy up, say, by an increase in the dose of irradiation, the rates of fragmentation of $ArX^{-\bullet}$ will equalize. The capture of $Ar^{\bullet}$ by a nucleophile will become a limiting stage and it cannot depend on the nature of a leaving group. In fact, the reactivity of phenyl iodide, phenyl chloride, phenyl fluoride, phenyltrimethylammonium iodide, and diphenyl sulfide toward a pair of nucleophiles $(EtO)_2PO^-K^+$ (p) and *tert*-$BuC(O)CH_2^-K^+$ (c) under conditions of sufficient irradiation are very close. The rate constant for the reaction with $(EtO)_2PO^-K^+$ (p) is denoted as k_p, and k_c is the rate constant of the reaction with *t*-$BuC(O)CH_2^-K^+$ (c). For all of the substrates, k_p/k_c (liquid ammonia, nitrogen atmosphere, at −40°C) is equal on average to 1.4; the deviation does not exceed 8–10% (Galli and Bunnett 1979, 1981).

The usually considered monomolecular mechanism of substitution implies that one-electron reduction activates a substrate sufficiently so that it can dissociate with no further assistance from a nucleophile. Next steps of the reaction consist of transformations of the resultant radical. However, in substrates having sp^3 carbon as a reaction center, influence of the leaving group has been fixed (Russell and Mudryk 1982a, 1982b). This led to the formulation of $S_{RN}2$ bimolecular mechanism of radical-nucleophilic substitution. In this mechanism, the initial products of single electron transfer are combined to form the product anion-radicals without formation of intermediate radicals. Scheme 4.13 gives a relevant example.

Other reactions with unusual effects of leaving groups (Amatore et al. 1982) also proceed according to $S_{RN}2$ mechanisms. The $S_{RN}2$ formulation and the concerned $S_{RN}1$ formulation are very close. What is important with respect to such reactions is that the stage of free radical formation is absent for them. Since free radicals are not present, solvents are acceptable even if they are good-hydrogen donors with no risk of breaking the radical chain.

4.3.4 Kinetic Approaches to Identification of Ion-Radical Reactions

4.3.4.1 Kinetic Isotope Effect

The rate constant of a reaction changes when an isotope replaces the atom participating in the reaction. Deuterium and tritium are the most commonly used isotopes, deuterium especially. The quantitative

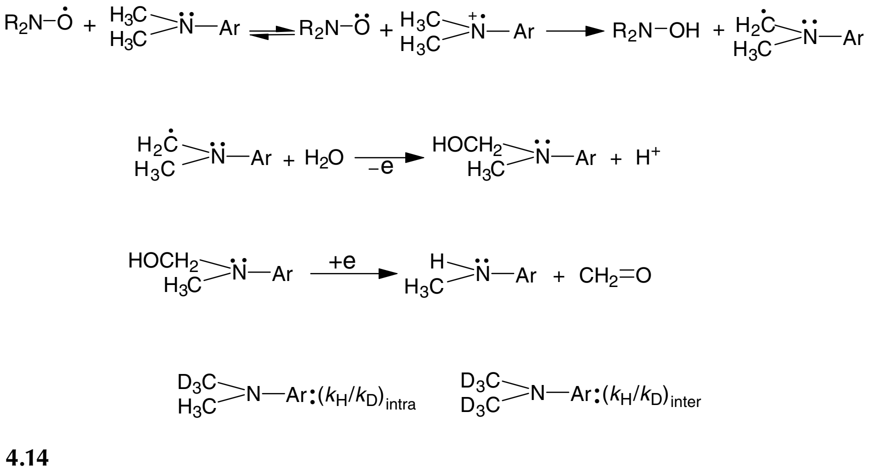
measure of kinetic isotopic effect is the ratio of reaction rate constants, for example, k_H/k_D. This effect proves conclusively that a particular atom is subject to attack and labeled bond participates in the limiting stage of a complex chemical reaction. The kinetic isotope effects as applied to ion-radical reactions have the following peculiarities. If ion-radical reactions proceed through elimination of a leaving group, then the kinetic isotope effect is observed, but it may not be addressed to the ion-radical nature of the reaction studied. However, the ion-radical reactions assume an electron transfer from a donor to an acceptor. An electron leaves the HOMO belonging to the whole donor molecule and populates the LUMO of the whole acceptor molecule. This process certainly differs from the substitution of atoms and groups. Thus, the direct connection between the heaviness of a leaving group and rate of its elimination cannot be the primary cause of the effect. At the same time, introducing a heavy atom into a donor or an acceptor molecule changes its ionization potential or electron affinity and has a definite influence over the electron-transfer rate constant. This phenomenon is detailed from theoretical and experimental standpoints in Section 2.6.

It is worthwhile mentioning here as a reminder that the reactions of electron transfer proceed through a polar transition state. Therefore, k_H/k_D for them depends, above all, on the dielectric constant of a solvent. This feature of the kinetic isotopic effect can really be used to establish the ion-radical stage, as it has been proven for reactions of phenylhydrazones with quinones (the employed solvents were DMSO, AN, THF, and dioxan; Rykova et al. 1980).

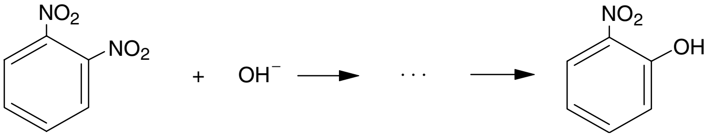
To discern the ion-radical nature of reactions, the so-called intramolecular and intermolecular proton/deuterium isotope effects may be of use. Baciocchi et al. (2005) revealed ion-radical mechanism for *N*-demethylation of *N*,*N*-dimethylanilines, $(CH_3)_2NAr$, by phthalimide-*N*-oxyl radical (Scheme 4.14). In this reaction, $(k_H/k_D)_{intra}$ values were derived for reactivity of $(CD_3)(CH_3)NAr$, whereas $(k_H/k_D)_{inter}$ was referred for the reactivity of $(CD_3)_2NAr$. The values of $(k_H/k_D)_{intra}$ were found to be always different and higher than $(k_H/k_D)_{inter}$. These results, although are incompatible with a single-step H-atom transfer from the N−C−H bond to the *N*-oxyl radical, were nicely interpreted on the basis of a two-step mechanism illustrated by Scheme 4.14. Namely, $(k_H/k_D)_{intra}$ is caused by an equilibrium in the formation of a primary *N*,*N*-dimethylarylamine cation-radical. The next step is irreversible and consists of proton transfer to produce an α-amino carbon radical. The latter stepwisely transforms into a demethylated final product.

4.3.4.2 Other Kinetic Approaches

A thorough investigation into the kinetics of a chemical reaction usually, although not always, determines its mechanism. With respect to ion-radical reactions, the substitution of the nitro group in *o*-DNB by the hydroxyl group is a relevant example as represented by Scheme 4.15.



SCHEME 4.14



SCHEME 4.15

For the nucleophilic substitution of Scheme 4.15, the following features have been established:

1. *o*-DNB reacting with OH^- in aqueous DMSO produces only *o*-nitrophenolate and nitrite (Abe and Ikegame 1976, 1978).
2. Mixing of the reactants quantitatively yields long-lived anion-radicals of *o*-DNB (Bil'kis and Shein 1975, Abe and Ikegami 1976, 1978).
3. Ion OH^- is indeed the donor of an electron within the system, and it converts into a short-lived radical $OH^•$ (Bil'kis and Shein 1975).
4. The pathway to *o*-nitrophenol (in the *o*-nitrophenolate form) proceeds through a σ-complex carrying the hydroxyl group at a tetrahedral carbon (Artamkina et al. 1982).
5. Initial *o*-DNB and the σ-complex do not exchange an electron (Abe and Ikegame 1976, 1978).
6. The first stage of *o*-DNB reaction with OH^- results in the formation of *o*-DNB anion-radical (Abe and Ikegame 1978).
7. The kinetic curve of the accumulation and consumption of *o*-DNB anion-radicals is S-shaped and that of the accumulation of *o*-nitrophenolate is parabolic. The anion-radical accumulation curve starts to go down when the *o*-nitrophenolate accumulation curve reaches its maximum (Abe and Ikegame 1978).
8. Kinetic calculations accord well with the experimental data only if *o*-DNB anion-radical is considered as the particle undergoing substitution of hydroxyl group for the nitro group (Abe and Ikegame 1978).

As seen, the results enumerated unambiguously support the anion-radical mechanism of this reaction. Despite the complexity of the problem, the kinetic approaches make its clarification quite possible. In all fairness, Tejero et al. (2005) wrote that these chains of proofs have not "resisted a close examination." However, Tejero et al. (2005) did not mention any refutations and this is a reason to include the foregoing eight (kinetic features) forcible arguments in our consideration. Contemporary works on nucleophilic substitution in DNBs accept Abe–Ikegami's mechanism. An example is the substitution of ethyl group for one of the nitro groups in *p*-DNB on action of triethylborane in the presence of potassium *tert*-butylate in *tert*-butanol (Palani et al. 2003).

Now let us turn to the stages of ion-radical conversion and try to estimate the activation barriers for each of the stages.

Initiation of the Ion-Radical Conversion

Generally, it is the interaction of a donor (D) and an acceptor (A) involving the transfer of one electron. The probability of one-electron transfer is determined by thermodynamics; namely, by the positive difference between the acceptor electron affinity and donor IP. The electron transfer is accompanied by a change in the solvate surroundings—charged particles are formed, and the solvent molecules (the solvent is usually polar) create a sphere around the particles thereby promoting their formation. Elevated temperatures destroy the solvate shell and hinder the conversion. Besides, electron transfer is often preceded by the formation of charge-transfer complexes by the sequence $D + A \rightarrow D \cdots A \rightarrow (D^{\delta+}, A^{\delta-}) \rightarrow (D^{+\bullet}, A^{-\bullet}) \rightarrow D^{+\bullet} + A^{-\bullet}$.

The formation of charge-transfer complexes presumes that donor and acceptor molecules are held in place by some forces. Here too, an increase in temperature hinders formation of complexes because it enforces the disorder of molecules in the solution. To summarize, the initial stage of the reaction (the ion-radical conception) has, as a rule, a negative temperature coefficient or, in any event, does not increase the total activation energy of the ion-radical reaction.

Development of the Ion-Radical Reaction

A profound rebuilding of a molecule, which is associated with bond cleavage, cannot take place at a negative or zero activation energy. Thus, disintegration of the anion-radicals of 4-iodo (or 4-bromo) nitrobenzene in AN or DMF proceeds with positive activation energy of 70–85 kJ · mol^{-1} (Parker 1981). The disintegration follows the equation:

$$4\text{-}O_2NC_6H_4I \rightarrow 4\text{-}O_2NC_6H_4^{\bullet} + I^-$$

As to the next step, namely, the reaction of aryl radicals with nucleophiles, we should take into account the fact that a π^* MO is available in the aryl halide to initially accommodate the incoming electron. The electron is subsequently transferred intramolecularly from the π^* to the σ^* MO of the carbon–halogen bond. Aryl radicals formed after carbon–halogen cleavage, effectively scavenge H-atoms. Therefore, an abstraction of a hydrogen atom from the solvent may occur. However, in the case of nucleophiles that can act as effective traps of aryl radicals, addition of a nucleophile to phenyl radical is predominant. At this point, let us focus on the step of nucleophile (Y^-) addition to the intermediate radical ($Ph^{\bullet}$). When a new σ-bond begins to form between the sp^3 carbon-centered radical ($H_5C_6^{\bullet}$) and Y^-, this bond is at first going to be a two-center, three-electron bond ($H_5C_6{\therefore}Y$). This process of nucleophile addition can and must be viewed as an inner-sphere electron transfer. In other words, formation of the new bond is concerted with the transfer of an electron to phenyl radical. Therefore, good-electron-donor character of Y^- is necessary for the efficiency of this step, the step leading to $(H_5C_6Y)^{-\bullet}$ as an anion-radical of final product. Galli and Gentili (1998) evaluated the thermodynamic driving force (TDDF) of the nucleophile/radical addition step. With respect to this step, they classified a nucleophile Y^- as good ($Y^- = {}^-CH_2COCH_3$, TDDF = −79.6 kJ · mol^{-1}), weak ($Y^- = {}^-SPh$, TDDF = −15.5 kJ · mol^{-1}), nonreactive ($Y^- = {}^-OPh$, TDDF = +21.4 kJ · mol^{-1}), and non-combined nucleophile ($Y^- = {}^-Br$, TDDF = +55.5 kJ · mol^{-1}). It is obvious that the additional steps with negative values of TDDF are thermodynamically favored.

In summary, when ion-radical substitution proceeds, it has only moderate activation energy and, if permitted thermodynamically, proceeds under mild conditions.

4.3.5 Positional Reactivity and Distribution of Spin Density in Substrate Ion-Radicals

ESR spectra of ion-radicals reveal the quantitative distribution of spin density. The ESR spectrum determines the HFC constant for the *i*th hydrogen, a_i^H. The constant is directly proportional to the spin density at the *i*th carbon carrying the *i*th hydrogen.

Of course, any correlation between a_i^H and the direction of, say, substitution does not prove that the reaction necessarily takes the ion-radical pathway. This means that the correlation may represent the relationship, for example, between the orientation and tendency of a substrate to locate a charge or between the electronic structure of the transition state and distribution of the spin density in the substrate ion-radical. Nevertheless, such correlation deserves to be considered; it can serve as one, but not single and self-sufficient, proof in favor of the ion-radical pathway.

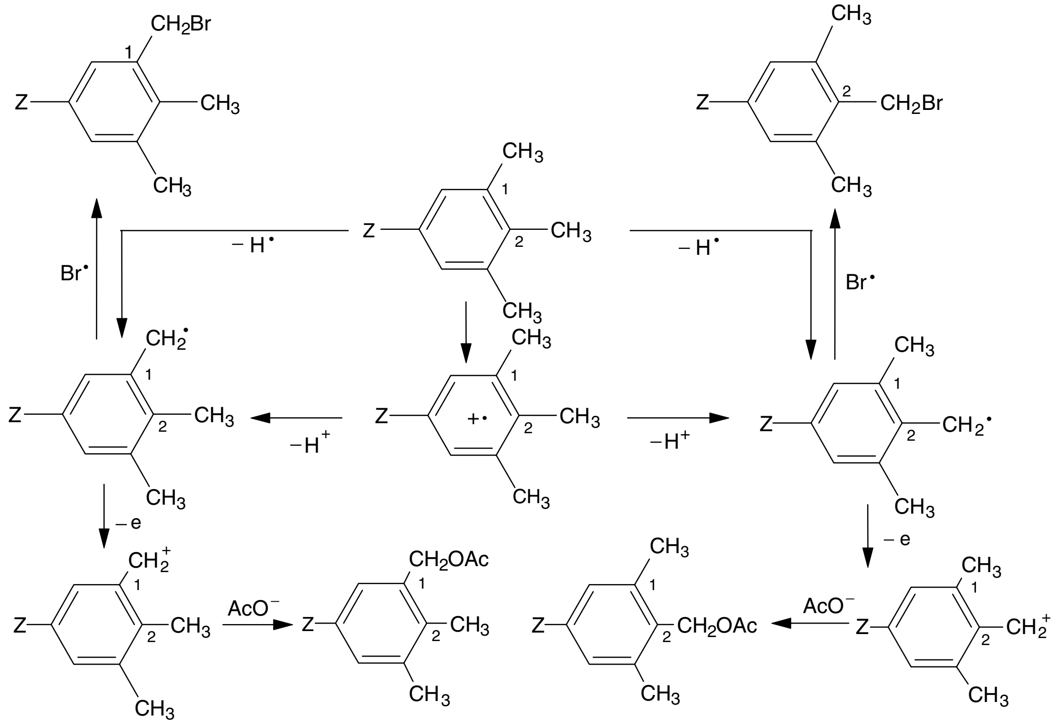
Let us first consider the intramolecular selectivity of out-of-ring substitution at 2 and 1 methyl groups in 1,2,3-trimethylbenzene derivatives. The k_2/k_1 ratio in Table 4.1 correlates with a_{Me}^H of the corresponding cation-radicals. Scheme 4.16 compares cation-radical and pure radical pathways of substitution in 1,2,3-trimethylbenzenes bearing a group Z in position 5 (Baciocchi 1995).

TABLE 4.1
Positional Selectivity (k_2/k_1) in Cation-Radical and Pure Radical Side-Chain Substitution of 5-Z-1,2,3-trimethylbenzenes

Reaction	k_2/k_1[a]				
	Z = Me	Z = *t*-Bu	Z = Br	Z = OAc	Z = Ome
CAN[b] in AcOH	55	24	42	100	>200
Anode oxidation in $AcOH/BF_4^{-}$[c]	37	16	31	59	
Anode oxidation in $AcOH/AcO^-$	16	8		41	>200
NBS + AIBN[d] in CCl_4	5	4	5	8	11

[a] k_2/k_1 is the reactivity ratio (statistically correct) of 2- and 1-methyl group in a substrate.
[b] CAN = cerium-ammonium nitrate, $(NH_4)_2Ce(NO_3)_6$; products are benzylic acetates.
[c] Products are benzylic acetates.
[d] NBS = *N*-bromosuccinimide, AIBN = azo*iso*butyronitrile; products are benzyl bromides.

Source: Baciocchi, E., *Xenobiotica* 25, 653, 1995.



SCHEME 4.16

Table 4.1 weighs the positional selectivity of the side-chain cation-radical acetoxylation against the side-chain pure radical bromination.

Table 4.1 compares two different reactions, namely, anode oxidation and oxidation with cerium ammonium nitrate (which are *bona fide* electron transfer processes) and bromination by *N*-bromosuccinimide in the presence of azobis(*iso*butyro)nitrile (which is a *bona fide* hydrogen-atom-transfer

process). Both electron-transfer and hydrogen-atom-transfer processes have the benzylic radical as a common intermediate, but positional selectivity is stronger for electron-transfer processes. An important point is the preference of the 2-positioned methyl group over the 1-positioned group, in terms of selectivity. For 1,2,3,5-tetramethylbenzene, such a preference reaches values from 16 to 55, and it is over 200 for 5-methoxy-1,2,3-tetramethylbenzene. As a second point, the selectivity factors mentioned are in accord with values of HFC constants in ESR spectra of corresponding cation-radicals. Thus, for the cation-radical of 1,2,3,5-tetramethylbenzene, HFC constant $a_{1\text{-Me}}{}^{H}$ = 0.3 mT, whereas $a_{2\text{-Me}}{}^{H}$ = 1.7 mT (Dessau et al. 1970). For *p*-methylanisole cation-radical, $a_m{}^{H}$ = 0.02 mT and $a_{p\text{-Me}}{}^{H}$ = 1.5 mT; for the anisole cation-radical, $a_m{}^{H}$ = 0.02 mT and $a_p{}^{H}$ = 1.06 mT (Dixon and Murphy 1976). Obviously, proton abstraction proceeds more easily from that position of a cation-radical where the spin (hole) density is maximal. This predetermines intramolecular selectivity in the cases of acetoxylation discussed.

Interesting data can also be cited on nucleophilic reactions. The relative rates of chlorine substitution in nitrochlorobenzenes under the action of different nucleophilic reagents accord well with $a_i{}^{H}$ of the anion-radicals. It is true that one is forced to rely on the values of $a_i{}^{H}$ not carrying chlorine. The spin of the chlorine nucleus and proton is 3/2 and 1/2, respectively. As a result, coupling at chlorine is 1/10 of that at the proton at the same spin density on the nucleus. In passing from nitrochlorobenzene to nitrobenzene, HFC constants of the corresponding anion-radicals practically do not change; see Table 4.2.

As seen from Table 4.2, activation energies of chlorine substitution in nitrochlorobenzenes under the action of diverse nucleophilic reagents are in agreement with $a_i{}^{H}$ of anion-radicals. Constants $a_2{}^{H}$ and $a_6{}^{H}$ of 4-chloronitrobenzene anion-radical are close to the $a_2{}^{H}$ and $a_6{}^{H}$ constants of nitrobenzene anion-radical. The anion-radicals of 2-chloronitrobenzene and nitrobenzene show the same agreement between $a_6{}^{H}$ and $a_4{}^{H}$. In the anion-radical of nitrobenzene, $a_4{}^{H}$ is greater than $a_2{}^{H}$. The substitution of ethoxyl for chlorine in 4-chloronitrobenzene proceeds much more easily and requires a lower activation energy than the same substitution in 2-chloronitrobenzene. The spin density in position 4 of the anion-radical of 1,3-DNB is greater than that in position 2 ($a_4{}^{H} > a_2{}^{H}$). Therefore, 1,3-dinitro-4-chlorobenzene is more active in nucleophilic substitution than 1,3-dinitro-2-chlorobenzene. For the anion-radical of 3-methylnitrobenzene, $a_6{}^{H}$ = 0.330 mT and $a_4{}^{H}$ = 0.488 mT (Geske et al. 1964). For the 3-nitrochlorobenzene anion-radical, $a_6{}^{H}$ = 0.320 mT and $a_4{}^{H}$ = 0.407 mT (Freed and Fraenkel 1964).

Table 4.3 presents the relative rate constants of the chlorine-to-methoxy substitution in the nitrobenzene series (Epiotis 1973). The methoxide ion replaces chlorine in 4-chloro-3-methylnitrobenzene more rapidly than in 6-chloro-3-methylnitrobenzene (Table 4.3, entries 1 and 2). This

TABLE 4.2
Constants HFC and Activation Energy in the Ethoxyl Group Substitution for Chlorine When Treating Nitro- and Dinitrochlorobenzenes with a Mixture of Ethyl Alcohol and Piperidine

Compound	Constant HFC (mT)	E_{act} (kJ · mol^{-1})
Nitrobenzene	$a_2{}^{H} = a_6{}^{H} = 0.330$, $a_4{}^{H} = 0.382$	—
2-Nitro-1-chlorobenzene	$a_6{}^{H} = 0.330$, $a_4{}^{H} = 0.392$	75.6
4-Nitro-1-chlorobenzene	$a_2{}^{H} = a_6{}^{H} = 0.342$	71.5
1,3-DNB	$a_2{}^{H} = 0.277$, $a_4{}^{H} = a_6{}^{H} = 0.449$	—
1,3-Dinitro-2-chlorobenzene	—	51.1
1,3-Dinitro-4-chlorobenzene	—	44.7

Source: For HFC constants, Fujinaga, T., Deguchi, Y., Umemoto, K. *Bull. Chem. Soc. Jpn*. **37**, 822, 1964. Freed, J.F. and Fraenkel, G.K., *J. Chem. Phys*., 41, 699, 1964. For values of E_{act}, Chapman, N.B., Parker, R.E., Soames, P.W., *J. Chem. Soc*., 2109, 1954.

agrees with the fact that the anion-radical of 3-methylnitrobenzene has a greater spin density in position 4 than in position 6. The same correlation is observed for HFC constants of 3-nitrochlorobenzene anion-radical and relative rate constants (k_{rel}) substitution of methoxyl for chlorine at the *i*th carbons (Table 4.3, entries 3 and 4).

Nucleophilic substitution reactions proceeding by the chain ion-radical mechanism also demonstrate correlation between the distribution of electron density in ion-radicals and reactivity of the corresponding uncharged substrates. As described earlier (Bunnett and Creary 1974b, Bunnett and Traber 1978), *m*-chloroiodobenzene reacts with such nucleophiles (Nu^-) as diethylphosphite and thiophenolate on photoirradiation in liquid ammonia. Under similar reaction conditions, monosubstitution yielding diethyl-*m*-chlorobenzene phosphonate prevails in the first case (Nu–diethylphosphite), whereas in the second case (Nu–thiophenolate) the main product is *m*-bis(phenylthio)benzene, the product of disubstitution. When the reaction involves diethylphosphite ion, a certain degree of disubstitution is achieved by lowering the concentration of the substrate. Thus, when the concentration of *m*-dichlorobenzene is 0.1 M, the reaction gives rise to the product of monosubstitution only. However, when this concentration is lowered to 0.008 M, disubstitution (up to 15%) proceeds concurrently with monosubstitution.

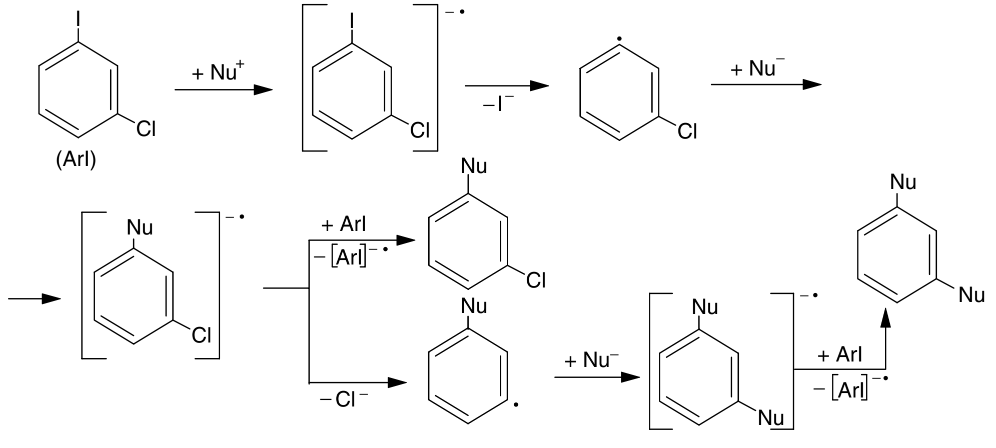
It is shown (Bunnett and Shafer 1978) that the products of thiophenolate and diethylphosphite disubstitution do not form from monosubstituted derivatives. The monosubstituted product is 20 times less active than the initial substrate with regard to thiophenolate. The $S_{RN}1$ model takes all these facts into consideration (see Scheme 4.17).

Scheme 4.17 shows that the course of the reaction is determined by the fate of the monosubstituted product in the anion-radical form. Because $(EtO)_2P(O)^-$ is a stronger acceptor than

TABLE 4.3
Relative Rate Constants of the Methoxy Ion Substitution for Chlorine (25°C, MeOH)

Entries	Nitrobenzene	Final Nitrobenzene	k_{rel}
1	6-Chloro-3-methyl-	6-Methoxy-3-methyl-	1
2	4-Chloro-3-methyl-	4-Methoxy-3-methyl-	3.6
3	3,6-Dichloro-	3-Chloro-6-methoxy-	1
4	3,4-Dichloro-	3-Chloro-4-methoxy-	2.6

Source: Epiotis, N.D., *J. Am. Chem. Soc.*, 95, 3188, 1973.



SCHEME 4.17

PhS-group, anion-radicals of $[m\text{-}ClC_6H_4SPh]^{-\bullet}$ decompose much more easily than anion-radicals of $[m\text{-}ClC_6H_4P(O)(OEt)_2]^{-\bullet}$. A more stable anion-radical exists until the moment it meets the initial substrate and gives the electron to it, thus producing a monosubstituted derivative. By contrast, a less-stable anion-radical cleaves the chloride ion before this anion-radical is subjected to one-electron oxidation, and the process tends toward disubstitution. The frequency of collisions of the chlorine-bearing anion-radical with the initial substrate is greater when the concentration of the substrate is higher. Therefore, diluting the solution promotes disubstitution. The ion-radical disubstitution also proceeds stepwise. It is important for our consideration that the second step involves the product in the anion-radical form, which is far more reactive than the corresponding uncharged molecule. Considered together, all these simple observations support the $S_{RN}1$ mechanism of the reaction.

In conclusion, it should be noted that it is necessary to check whether the $S_{RN}1$ mechanism is operative when passing from one reaction system to another, even if they are similar.

Thus, ketone enolates easily substitute chlorine in position 2 of the electrophilic nucleus of pyrazine (1,4-diazabenzene), and even in the dark, the reaction proceeds via the $S_{RN}1$ mechanism (Carver et al. 1981). It is expected that the introduction of the second chlorine in the ortho position to 4-nitrogen in the electrophilic nucleus of pyrazine promotes the ion-radical pathway even more effectively. However, 2,6-dichloropyrazine in the dark or subjected to light reacts with the same nucleophiles by S_N2 and not $S_{RN}1$ mechanism (Carver et al. 1983). The authors are of the opinion that two halogens in the pyrazine cycle facilitate the formation of σ-complex to the extent that dehalogenation of anion-radicals in solution and a subsequent nucleophilic attack of free pyrazine radical become virtually impossible. Thus, the reaction may either involve or exclude the intermediate σ-complex, and only special identification experiments can tell which is the true one.

It is worth noting that the correlation between the spin densities in ion-radicals and selectivity in their reaction of substitution has no value unless combined with other proof. However, such correlations may contribute to elucidation of the real mechanism.

4.3.6 Identification by Methods of Chemical Probes

4.3.6.1 Initiation of Polymerization of Vinyl Additives

If free radicals are formed during a reaction including an electron-transfer stage, they are revealed through their initiation of polymerization of vinyl additives. The vinyl compounds act, therefore, as chemical probes. Thus, the reaction of sodium thiophenolate with alkyl or benzyl halides proceeds through a stage of electron transfer producing the phenylthiyl radical. This radical is unstable, but it can be trapped by introducing styrene into the reaction system. Even minute quantity of the phenylthiyl radical is sufficient to initiate styrene polymerization. The polymerization proceeds with the insertion of phenylthiyl fragments. In the corresponding experiment, the sulfur-containing oligomer was separated and characterized (Flesia et al. 1978). The oligomer does not form when thiophenolate is mixed with styrene in the absence of the acceptor component (alkyl or benzyl halide). The introduction of the radical trap—phenyl-*tert*-butyl nitrone—decelerates the reaction of the acceptor component with thiophenolate. ESR spectroscopy registers the product of the phenylthiyl radical addition to nitrone. This indicates that phenylthiyl radicals are formed on the main pathway of the reaction as follows:

$$PhSNa + PhCH_2Hal \rightarrow PhS^\bullet + [PhCH_2Hal]^{-\bullet}Na^+ \rightarrow NaHal + PhSCH_2Ph$$

In the same manner, appearance of phenyl radicals, $C_6H_5^\bullet$, in the course of substitution of a nitro group for a diazonium group has been demonstrated in the reaction of benzene diazonium salts with sodium nitrite. Acrylonitrile introduced into the reaction mixture polymerizes; the polymerization takes place in nitrogen, and oxygen inhibits it (Singh et al. 1982). This supports the ion-radical mechanism of the reaction. However, the initiation alone (of polymerization of vinyl compounds) cannot be regarded as sufficient proof of the ion-radical pathway of the reaction. In the same paper, Singh et al. (1982)

reported that benzene- and *p*-nitrobenzene diazonium fluoroborates are converted into nitro- and *p*-dinirtobenzene under the action of sodium nitrite in methanol, whereas *p*-methoxybenzene diazonoium does not produce *p*-nitroanisole. The fact that *p*-methoxybenzene diazonium falls out of the series is easily explained—the *p*-methoxyphenyl radical is incapable of coupling with nitrite ion, and the sequence of stages needed for the ion-radical reaction is interrupted.

Now, the separation of polymers from the reaction mixture containing the vinyl additive indicates that the substrate produces a radical at the intermediate stage. The radical produced adds to a "probe" molecule and forms an adduct with the vinyl monomer, that is, initiates the monomer polymerization. Sometimes, however, the polymerization does not start but the reaction yields a low-molecular-weight individual substance containing fragments of substrate, an added monomer, and reactant. To illustrate, let us consider the following reaction of perfluoroalkyl iodide (substrate) with nitropropenide salt (reactant) in the presence of a monomer probe (vinyl acetate, methylmethacrylate, and styrene) (Feiring 1983):

$$C_6F_{13}I + [Me_2CNO_2]^- \; Bu_4N^+ \rightarrow Bu_4NI + (C_6H_{13}^\bullet, Me_2C^\bullet NO_2)$$

$$(C_6H_{13}^\bullet, Me_2C^\bullet NO_2) \rightarrow C_6H_{13}C(NO_2)Me_2$$

$$(C_6H_{13}^\bullet, Me_2C^\bullet NO_2) + PhCH{=}CH_2 \rightarrow C_6F_{13}CH_2CH(Ph)C(NO_2)Me_2$$

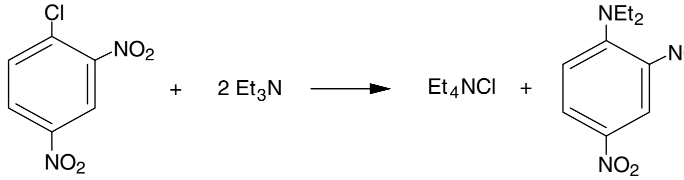
In this case, the initial donor–acceptor interaction yields radicals of identical activity. The presence of styrene gives rise not to a polymer but to a low-molecular individual compound containing fragments of the probe and both radicals formed.

4.3.6.2 Method of Inhibitors

Each ion-radical reaction involves steps of electron transfer and further conversion of ion-radicals. Ion-radicals may either be consumed within the solvent cage or pass into the solvent pool. If they pass into the solvent pool, the method of inhibitors will determine whether the ion-radicals are produced on the main pathway of the reaction, that is, whether these ion-radicals are necessary to obtain the final product. Depending on its nature, the inhibitor may oxidize the anion-radical or reduce the cation-radical. Thus, quinones are such oxidizers whereas hydroquinones are reducers. Because both anion and cation-radicals are often formed at the first steps of many ion-radical reactions, quinohydrones—mixtures of quinones and hydroquinones—turn out to be very effective inhibitors. Linares and Nudelman (2003) successfully used these inhibitors in studies on the mechanism of reactions between carbon monoxide and lithiated aromatic heterocycles.

Nucleophilic substitution of chlorine in 2,4-dinitrochlorobenzene by diethylamino group from triethylamine (Scheme 4.18) is a rare example when both the formed opposite-charged ion radicals exist together in the bulk solution for a long time.

The anion-radical of 2,4-dinitrochlorobenzene and cation-radical of triethylamine pass into the solvent volume. In this case, both acceptors (*p*-BQ, tetracyanoethylene, and tetracyanoquinodimethide) and donors of an electron (potassium iodide, ferrous sulfate, and *N*,*N*-tetramethyl-*p*-phenylenediamine) inhibit substitution (Shein 1983).



SCHEME 4.18

Frequently, a substrate anion-radical quickly decomposes, giving off the organic radical, and only then transforms into the final product. In this case, usual inhibitors of radical reaction are employed and the reaction mechanism is disclosed from the nature of the products. Thus, the transfer of an electron from the anion-radical of naphthalene to organomercury halides gives naphthalene and substrate anion-radical. The latter decomposes in two stages—$[RHgHal]^{-\bullet} \rightarrow Hal^- + RHg^\bullet$ and $RHg^\bullet \rightarrow Hg + R^\bullet$. Then, symmetrization proceeds as follows:

$$R^\bullet + RHgHal \rightarrow [R_2HgHal]^\bullet$$

$$[R_2HgHal]^\bullet + e \rightarrow [R_2HgHal]^{-\bullet}$$

$$[R_2HgHal]^- \rightarrow Hal^- + R_2Hg$$

Cumene ($H^\bullet$ donor) inhibits the symmetrization. The main direction becomes the reductive demercurization because the radicals, $R^\bullet$, controlling the process leave the sphere of the reaction: $R^\bullet + H^\bullet \rightarrow RH$ (Singh and Khanna 1983).

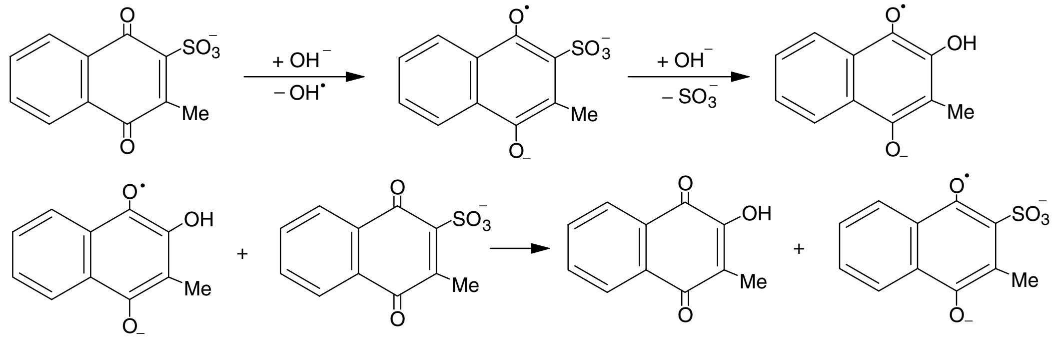
Widely encountered are the reactions, which produce $^\bullet OH$, $^\bullet OAlk$ unstable radicals from reactants ^-OH, ^-OAlk and rather stable anion-radicals from substrates, say, quinones. The radicals are revealed by radical interceptors and the anion-radicals are disclosed with the help of inhibitors (oxidizers). Radical interceptors is considered in Section 4.3.6.3; here attention is drawn to inhibitors.

Sodium methylate acting on 2-chloroanthraquinone substitutes the methoxy group for chlorine and produces anion-radicals of the substrate (Shternshis et al. 1973). The study of kinetics has demonstrated that the amount of substrate anion-radical first increases and then sharply decreases. The inhibitor (*p*-BQ) decelerates the formation of anion-radicals. The rate of formation of 2-methoxyanthraquinone also decreases. If anion-radicals are produced on the side pathway, the rate of formation of the end product on introduction of the inhibitor should not have decreased. Moreover, it should even rise because oxidation of anion-radicals regenerates uncharged molecules of the substrate. Hence, the anion-radical mechanism controls this reaction.

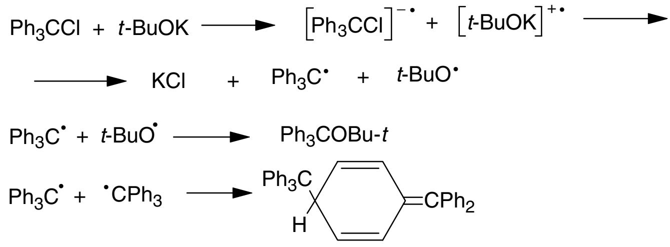
As described, other nucleophilic reactions in the anthraquinone series also involve the production of anion-radicals. These reactions are as follows: Hydroxylation of 9,10-anthraquinone-2-sulfonic acid (Fomin and Gurdzhiyan 1978); hydroxylation, alkoxylation, and cyanation in the homoaromatic ring of 9,10-anthraquinone condensed with 2,1,5-oxadiazole ring at positions 1 and 2 (Gorelik and Puchkova 1969). These studies suggest that one-electron reduction of quinone proceeds in parallel to the main nucleophilic reaction. The concentration of anthraquinone-2-sulfonate anion-radicals, for example, becomes independent of the duration time of the reaction with an alkali hydroxide, and the total yield of the anion-radicals does not exceed 10%. Inhibitors (oxygen, potassium ferricyanide) prevent formation of anion-radicals, and the yield of 2-hydroxyanthraquinone even increases somewhat. In this case, the anion-radical pathway is not the main one. The same conclusion is made in the case of oxadiazoloanthraquinone.

Therefore, only when it is strongly grounded, can the anion-radical stage be included in the mechanism of a reaction. At this point, it is interesting that another representative of sulfonated quinones, sodium 3-methyl-1,4-naphthoquinone-2-sulfonate, substitutes the hydroxy group for the sulfonate fragment mainly by ion-radical mechanism. The initial stage involves formation of substrate anion-radicals, and the end product is 2-hydroxy-3-methyl-1,4-naphthoquinone. As the reaction proceeds, the quantity of anion-radicals reaches a maximum, and then abruptly drops. At this moment, the concentration of the end product starts to grow. On addition of inhibitors (oxygen, potassium ferricyanide), the anion-radicals do not accumulate and end products do not form. This indicates that hydroxylation of 3-methyl-1,4-naphthoquinone-2-sulfonate proceeds at the expense of ion-radicals via the chain mechanism (Fomin and Gurdzhiyan 1970) (Scheme 4.19).

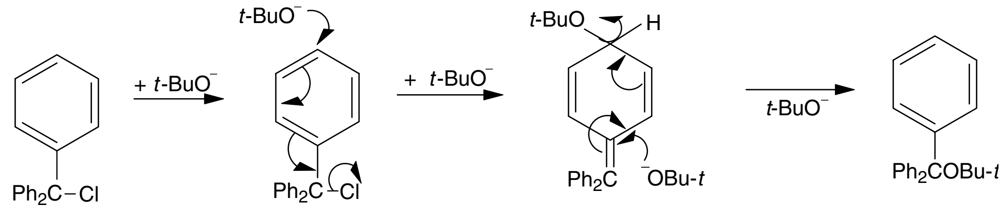
The method of inhibitors has demonstrated that substitution of chlorine in triphenylchloromethane by *tert*-butoxy anion does not follow anion-radical mechanism. This mechanism is widely accepted for the reactions shown in Scheme 4.20 (Bielevich et al. 1968, Ashby et al. 1981).



SCHEME 4.19



SCHEME 4.20



SCHEME 4.21

This widely accepted mechanism postulated the formation of radical pair followed by carbon–oxygen bond formation within the pair. When the solution of triphenylmethyl chloride in THF was mixed with potassium *tert*-butylate in the radiospectrometer cavity, the ESR spectrum visualized the presence of triphenylmethyl radical. The intensity of this signal first increased reaching a maximum and then decreased to an equilibrium value. In the opinion of Bielevich et al. (1968), the superequilibrium concentration of the radicals agreed well with their generation at the primary stage of one-electron transfer. In other words, the substitution product supposedly is formed at the expense of the primary generated radicals. The ESR spectrum fixed those triphenylmethyl radicals that failed to recombine with *tert*-butoxyl radicals before their passage into the solvent pool.

However, when *m*-DNB was added to a solution of triphenylchloromethane and potassium *tert*-butylate in 2,2-dimethoxypropane, the yield of the substitution product and dimer of the triphenylmethyl radical markedly increased and decreased, respectively (Simig and Lempert 1979). Therefore, the main pathway of the reaction does not involve the ion-radical step. These authors suggested an alternative pathway, which is conformed by a thorough structural analysis of the secondary products formed along with *tert*-butyl ester of triphenylcarbinole (Huszthy et al. 1982a, 1982b) (Scheme 4.21).

4.3.6.3 Method of Radical and Spin Traps

The aim of this section is to give a concise description of the use of traps, note the most popular and newly recommended traps, as well as underline the possible artifacts connected with the trap applications to ion-radical reactions. There are traps for ion-radicals and neutral radicals resulting from ion-radical disintegration.

Thus, 3,4-dihydroxybenzoic acid is an effective trap for cation-radicals such as the cation-radical from 2,2′-azino-bis[3-ethylbenzothiazoline-6-sulfonic acid] (Lee et al. 2006). In this case, trapping leads to cation-radical decolorization measured by a diminution of optical absorption.

The problem of radical trapping is also relevant because radicals are often the primary products of ion-radical transformations. The radicals are, as a rule, not stable, and special traps—*radical* and *spin*—are used to reveal them.

Radical traps belong to the class of stable free radicals, for example, of the nitroxyl or phenoxyl type. Interacting with radicals produced by a reaction, radical traps give diamagnetic compounds. One can follow the progress of the reaction by a decreasing intensity of the ESR spectrum of the radical trap.

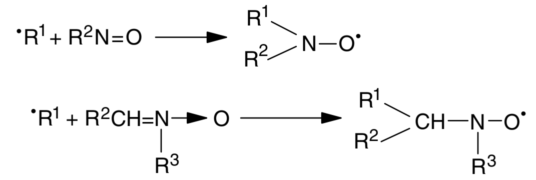
Nitroso compounds, nitrones, and other diamagnetic molecules are used as spin traps. Capturing radicals produced in the reaction, spin traps form the so-called spin adducts—stable nitroxyl radicals easily detectable by ESR spectroscopy. In other words, the progress of the reaction can easily be followed by an increasing intensity of the spin-adduct signal. By and large, the method of traps reveals radicals by the disappearance (or appearance) of the ESR signal.

Radical and spin traps can inhibit the observed conversions, and this is their common drawback. Chain reactions can be inhibited either at the stage of generation or branching. A portion of radicals, which combines with trap molecules, leaves the sphere of a reaction. Even small amounts of a trap can affect the kinetics of reaction if it proceeds via a chain mechanism. Traps can exchange electrons with initial anion-radicals or with the anion-radicals of a product. As a result, spin traps are converted to paramagnetic species, which distort the spectral picture. In cases of radical traps, capturing an electron produces diamagnetic compounds before combining with radicals, and ESR spectra cannot be observed. Even when a radical trap has an additional group with strong electron affinity, a biradical is not formed and so no ESR signal can be generated. Thus, piperidone nitroxyl in the presence of cyclooctatetraene dianion undergoes one-electron reduction at the site of a free valence without the participation of carbonyl group. In other words, the anion of corresponding hydroxylamine is formed instead of the nitroxyl bearing the ketyl group (Todres 1970).

Let us now consider features of trap employment in cases, which are free from masking effects.

Radical traps. The kinetics of a decrease in the ESR signal intensity represents the kinetics of radical generation in the reaction mixture, because the adduct forms rapidly at a rate of diffusion. Later, several examples of applications of radical traps in kinetic studies are cited.

Spin traps. Nitroso compounds and nitrons (*N*-oxides) interact with radicals to form nitroxyl radicals (Scheme 4.22).



SCHEME 4.22

This usage is based on the fast reaction between a suitable diamagnetic molecule (a spin trap) and short-lived free radicals with the formation of relatively long-lived radicals (spin adducts) whose ESR signals are persistent enough to be recorded and analyzed. HFC constants and *g*-factors of the spin adducts are characteristic of the type of initial radical trapped. Thus, the coupling constant, a^N, depends on the nature of groups bonded to nitrogen. Coupling constants for nitroxyl radicals vary over a wide range from 0.4–0.5 mT for diacylnitroxyls (Lemaire et al. 1965) to 2.5–2.8 mT for alkoxynitroxyls (Rehorek 1980). Changes in these coupling constants after the spin-adduct formation provide information on the nature of a short-lived radical fixed by a trap.

Examples of Spin Traps

1. The most universal and therefore most commonly used traps are nitroso-*tert*-butane and di(*tert*-butyl)nitroxide (Wajer et al. 1967, Arguello et al. 2000). Usually, radicals combining with these traps produce stable and well identifiable spin adducts. When studying the ion-radical reactions, which involve prolonged heating or light irradiation, one should keep in mind that the trap decomposes based on these conditions according to the following equations:

$$Me_3CN{=}O \rightarrow Me_3C^\bullet + {}^\bullet NO$$

$$Me_3C^\bullet + Me_3CN{=}O \rightarrow (Me_3C)_2N{-}O^\bullet$$

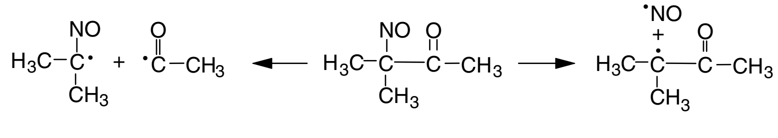
   As per this scheme, the *tert*-butyl radical adds to the initial nitroso trap producing the nitroxyl radical. A triplet in ESR spectra with $a^N = 1.5–1.7$ mT (depending on the solvent) corresponds to the radical. The triplet is often so intense that it can lap over signals from other spin adducts (Forshult et al. 1969).

2. 2-Methyl-2-nitrosobutanone-3 exists in the nonactive form of a dimer. The dimer dissociates in solution to give a monomer. Light irradiation or heating promotes the dissociation, causing at the same time the decomposition of the monomers into radicals according to Scheme 4.23.

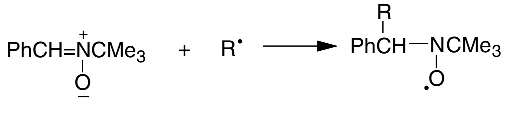
   Thus the radicals produced add to the initial molecule of a trap giving spin adducts. The nitrogen coupling constants of these spin adducts lie in the ESR regions of 1.4–1.5 and 0.7–0.8 mT (Torsell 1970, Janzen 1971, Lagercrantz 1977).

3. *C*-Phenyl-*N*-*tert*-butylnitrone [$PhCH{=}N^+(^tBu)O^-$] is rather stable. The formation of its spin adducts is illustrated in Scheme 4.24 (Sang et al. 1996, references therein).

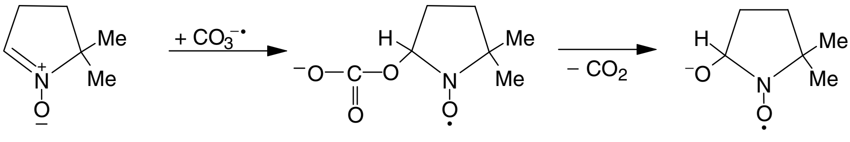
   In the spin adducts of Scheme 4.24 (this is an essential feature), the unpaired electron interacts not only with the nitrogen nucleus but also with the nucleus of the hydrogen of



SCHEME 4.23



SCHEME 4.24



SCHEME 4.25

CH fragment neighboring the nitrogen [R^1R^2CH–$N(R^3)$–$O^•$] (Janzen and Blackburn 1969). This extends the identification possibilities of nitrone as a spin trap.

In this type of spin traps, 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO) deserves particular mention. DMPO is widely employed as a spin trap in the detection of transient radicals or ion-radicals in chemical and biological systems (see, e.g., Siraki et al. 2007). Characteristic ESR spectra arising from the formation of spin adducts are used for identification of specific spin species. In common opinion, such identification is unambiguous. However, in reactions with superoxide ion (Villamena et al. 2004, 2007b), carbon dioxide anion-radical (Villamena et al. 2006), or carbonate anion-radical (Villamena et al. 2007a), this spin trap gives rise to two adducts. Let us consider the case of carbonate anion-radical. The first trapped product arises from direct addition of carbonate anion-radical, second adduct arises from partial decarboxylation of the first one. Scheme 4.25 illustrates such reactions based on the example of carbonate anion-radical.

DMPO finds a very wide usage because it is a particularly reactive radical scavenger and gives persistent spin adducts, with useful information derived from nitrogen and β-hydrogen splittings. These splittings appear within a broad range, facilitating the spectral interpretation (Cano et al. 1999). Special efforts are, however, directed to search of DMPO analogs having no β-hydrogen to nitrone function (e.g., Astofi et al. 2007). Adducts containing β-hydrogen, although differing with widened informativity of their ESR spectra, are prone to disproportionate giving of DMPO and a hydroxylamine. The use of DMPO is also limited by its sensitivity to nucleophile attack. Phosphororganic derivatives of DMPO give a good alternative because they form spin adducts with prolonged lifetimes (Hardy et al. 2007).

4. Nitrosobenzenes are commonly used as spin traps. They are stable and convenient to identify radicals (Zuman and Shah 1994). Most often, however, not nitrosobenzene itself but its 2,4,6-trimethyl and 2,4,6-tri(*tert*-butyl) derivatives are utilized for this purpose; sometimes 2,3-dichloro- and 2,6-dichloronitrosobenzenes can be used. Nitrosobenzenes, ArN=O, have a wider application than other traps. This is explained by the fact that the structure of spin adducts strongly depends on the nature of the added radical. Some radicals can form Ar-$N^•$-OR adducts, others form ArN($O^•$)R adducts.

The main advantage of nitrosobenzenes as compared to nitrones is that a radical is added to nitrogen or oxygen rather than to carbon, as in nitrones. This gives more direct information on the structure of the radical trapped. Spin adducts with nitrosobenzenes differ in the *g*-factor and can be distinguished (Terabe and Konaka 1971, Terabe et al. 1973). The primary alkyl radicals and aryl and arylthio radicals form spin adducts with a free valence at nitrogen, tertiary radicals produce spin adducts with a free valence at oxygen, and secondary radicals give both types of adducts.

The application of nitrosobenzenes has a number of peculiarities. First, nitrosobenzene also may add a nucleophilic agent (Nu^-). The product of this addition easily oxidizes to generate radical PhN(Nu)$O^•$. This causes errors in assigning the reaction to an ion-radical type. To avoid this, Lagercrantz (1977) suggested the use of derivatives wherein the nitrogen of nitroso group is sterically hidden. In these spin traps, only oxygen of the nitroso group can react and only when attacked by radicals.

Second, nitrosobenzenes can give spin adducts interacting with solvents without the participation of reactants or substrates. Compounds of the nitrosobenzene series react in

such solvents as *n*-decane, ethylbenzene, *iso*-propylbenzene, and *o*-xylene (Simon et al. 1980). The following reactions proceed with *n*-decane as an example:

$$C_{10}H_{22} + ArN{=}O \rightarrow C_{10}H_{21}^{\bullet} + ArN(O^{\bullet})H$$

$$C_{10}H_{21}^{\bullet} + ArN{=}O \rightarrow ArN(O^{\bullet})C_{10}H_{21}^{\bullet}$$

These aggravating reactions proceed at room temperature or under moderate heating up to 60°C without light excitation and in the absence of oxygen, that is, in conditions common to electron-transfer reactions. (Some of these reactions just take place in nonpolar solvents of the decane or xylene type.) Hence, application of nitrosobenzene as spin traps can be complicated by solvent participation.

The method of spin traps is used to perform not only qualitative but also quantitative measurements. For quantitative determinations, the spin-trap method is applied if the rate constant of radical initiation is 10^7–10^8 L · mol^{-1} · s^{-1} and trap concentration is not below 10^{-2} M (Freidlina et al. 1979).

Participation of Traps in Redox Reactions

This problem has two aspects—consumption of spin traps in one-electron oxidation/reduction either of a free radical or an initial ion-radical. An electron exchange between a trap and radical depends on a relative rate of the exchange as compared to rates of the addition reactions considered. An electron exchange between a trap and an ion-radical is represented by the following sequence (Nu^- is a nucleophile):

$$R^1X + Nu^- \rightarrow (R^1X)^{-\bullet} + Nu^{\bullet}$$

$$(RX)^{-\bullet} + AlkN{=}O \rightarrow RX + (AlkN{=}O)^{-\bullet}$$

$$(RX)^{-\bullet} \rightarrow R^{\bullet} + X^{-\bullet}$$

$$R^{\bullet} + Nu^- \rightarrow (RNu)^{-\bullet}$$

$$(RNu)^{-\bullet} + AlkN{=}O \rightarrow RNu + (AlkN{=}O)^{-\bullet}$$

Electron Exchange between a Trap and Free Radical

A trap and an unstable radical can, in general, form an adduct as discussed earlier. Electron transfer can yield a pair of a cation (from a radical) and an anion-radical (from a trap) or a pair of an anion (from a radical) and a cation-radical (from a trap). All of these reactions are possible and, indeed, take place under certain conditions. Some radicals either do not form adducts with traps or form them in extremely low yields. Therefore, the method fails to give information in cases where it should be effective. For example, Sosonkin et al. (1982) failed to reveal $RCH^{\bullet}OH$ radicals by means of PhN=O. This result becomes understandable when comparing the rate constants of the corresponding processes. Namely, the rate constant of radical addition to the trap is 10^3–10^8 L · mol^{-1} · s^{-1}, and the rate constant of electron transfer from $RCH^{\bullet}OH$ to PhN=O is 10^9–10^{10} L · mol^{-1} · s^{-1}. It is readily apparent that the addition of the radical cannot compete with one-electron transfer. Sosonkin et al. compared the redox potentials of a number of free radicals and spin traps; they demonstrated that the nitroso compounds capture quantitatively only radicals having oxidation potentials below 0.6 V. These radicals are $Alk^{\bullet}$, $Ph^{\bullet}$, $RO^{\bullet}$, $HO^{\bullet}$, $^{\bullet}CH_2COOH$, $^{\bullet}CH_2COR$, and some others. Nitrones, however, are reduced at extremely negative potentials and cannot capture electrons even from the strongest reducers—ketyl anion-radicals $(R^1R^2C{=}O)^{-\bullet}$. Consequently, nitrones can be used widely for quantitative intercepting of radicals even if they are liable to one-electron oxidation.

So far we have considered the acceptor properties of spin traps. Their donor properties are also known, although they are studied to a lesser extent. The literature data are scarce, and only several

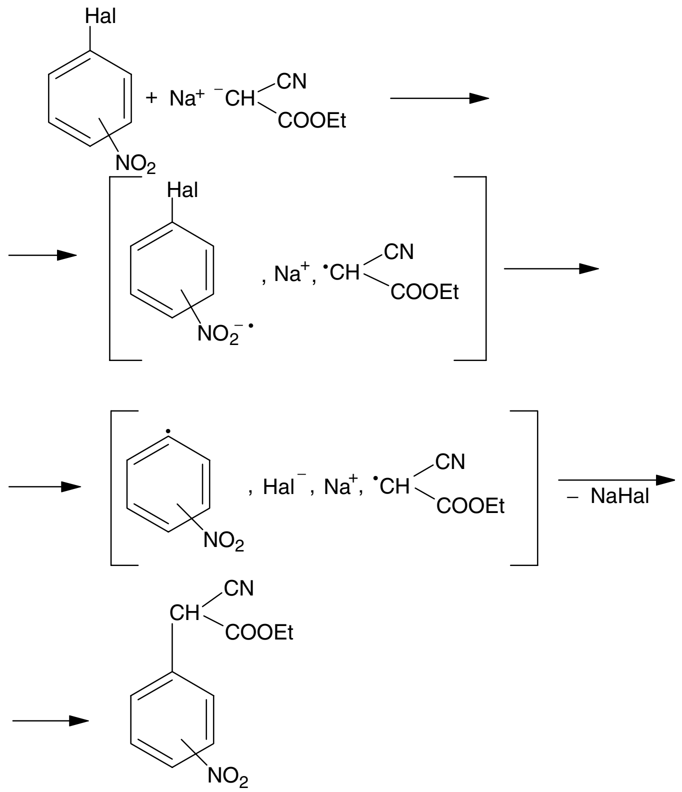
examples of one-electron oxidation of traps can be cited. Nitrosodurene forms stable cation-radicals on photolysis in the presence of Ce^{4+} and U^{6+} in CF_3COOH (Rehorek 1979). Murabayashi et al. (1979) observed the formation of cation-radicals from 2,4,6-tris(*tert*-butyl)nitrosobenzene subjected to the action of 3-methylpentane molecular cation.

While using the trap method, one should take into account the oxidation properties of a trap with respect to radicals or other electron donors that are present in the system. Because spin traps can be electron donors themselves, their oxidation potentials should be more positive than that of the participants of the reaction under study.

Electron Exchange between a Trap and the Initial Ion-Radical

Spin traps can act as one-electron oxidizers. This property is even more pronounced in the interactions of traps with anion-radicals. Traps can block the ion-radical pathway. In other words, they inhibit the whole reaction, including the ion-radical step. This can be explained by both the oxidation of substrate anion-radical and chain termination due to oxidation of product anion-radical. An illustrative example is the inhibition of $S_{RN}1$ nucleophilic substitution of 2-chloroquinoxaline by the radical trap bis(*tert*-butyl)nitrone (Carver et al. 1982).

The yields of reaction products from thermal nucleophilic substitution reactions in DMSO of *o*- and *p*-nitrohalobenzenes (Zhang et al. 1993) or *p*-dinitrobenzene (Liu et al. 2002) with the sodium salt of ethyl α-cyanoacetate were found to be markedly diminished from the addition of small amounts of strong electron acceptors such as nitrobenzenes. At the same time, little or no diminution effects on the yields of the reaction products were observed from the addition of radical traps such as nitroxyls. These results are consistent with the conclusion that such reactions proceed via a nonchain radical nucleophilic substitution mechanism (Scheme 4.26).



SCHEME 4.26

In Scheme 4.26, the nonchain mechanism explains the failure of the radical traps to affect the yield of the reaction. According to this mechanism, the reactive radical intermediates are held within the solvent cage. Evidently, the radical traps cannot penetrate the solvent cage like an electron can. In other words, the radical traps present in the solution, even in great excess, cannot intercept the radicals in the framework of the nonchain radical mechanism. Galli (1988a) provided other similar examples of this phenomenon.

4.4 PHYSICAL APPROACHES TO IDENTIFICATION OF ION-RADICAL REACTIONS

Preceding sections of this chapter described the substances taking part in ion-radical conversions and analyzed the resulting products. However, to get deeper insight into the course of the process, it is necessary to reveal intermediate species participating in conversions. When ion-radicals are formed, they are discovered by numerous physical methods.

4.4.1 Radiospectroscopy

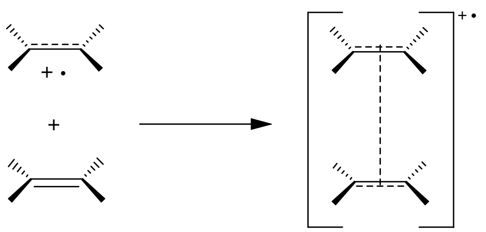
4.4.1.1 Electron Spin Resonance Methods

ESR methods unambiguously establishes the presence of species bearing unpaired electrons (ion-radicals and radicals). The ESR spectrum quantitatively characterizes the distribution of electron density within the paramagnetic particle by a hyperfine structure of ESR spectra. This establishes the nature and electronic configuration of the particle. A review by Davies (2001) is highly recommended as "a guide to current practice for ESR spectroscopic studies" (this quotation is from the title of the review). The ESR method dominates in ion-radical studies. Its modern modifications, namely, ENDOR and electron–nuclear–nuclear triple resonance (TRIPLE) and special methods to observe ion-radicals by swiftness or stealth are described in special literatures (Moebius and Biehl 1979, Kurreck et al. 1988, Werst and Trifunac 1998).

The ESR method provides information only on particles, which exist for more than 1×10^{-3} s. To investigate short-lived radicals, ESR spectra are recorded in a steady flow. The steady-flow methods allow one to study reactions with conversion times below 10^{-4} s. Therefore, an apparent failure to observe aimed intermediates by ESR method should not discourage a researcher. Simply another method should be chosen. Thus, bicyclopropyilidene after one-electron oxidation gives rise to tetramethylene ethane cation-radical. The latter exists in two interconvertible isomers that differ in the character of their single-occupied molecular (SOMO) orbitals and torsion angle between the two resulting allyl fragments. The ESR method is unable of establishing existence of these somomers, but near-IR absorption method can do it (Mueller et al. 2003).

To investigate multispin systems, the so-called electron spin transient nutation (ESTN) spectroscopy is recently elaborated. This is a version of pulsed ESR. Nutation is the precessional motion of spin. The method and its applications are detailed in the paper of Itoh et al. (1997). Chapters 1 and 8 describes that the determination of spin multiplicity becomes a very important problem in organic chemistry of ion-radicals.

In the last few years, time-resolved fluorescence, optically detected ESR (OD ESR), and magnetically affected reaction yield (MARY) (Kalneus et al. 2005, 2006) spectroscopy are finding ever-increasing use. Other spin-analyzing methods, already mentioned here, deal with those ion-radicals that live long enough to be fixed in the appropriate scale of time. By using OD ESR and MARY, it is possible to fix ion-radicals whose living time is extremely short, down to nanoseconds (Borovkov et al. 2007). It is also possible to follow the ion-radical disappearance at the expense of reactions with other partners or solvent molecules (Sviridenko et al. 2001, V'yushkova et al. 2006) or pseudorotation as in the case of 1,2,3-trifluorobenzene anion-radical (Barlukova et al. 2005, V'yushkova et al. 2005).



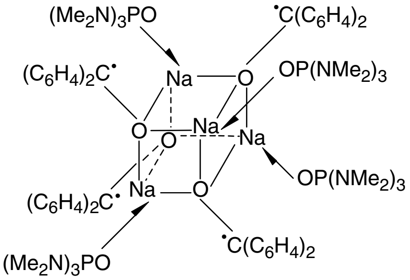
SCHEME 4.27

Experimentally, a solution containing a solvent (alkane, Alk), donor (D), and an acceptor (A) is exposed to X-ray irradiation. The sample to be studied is placed in a magnetic field, and its fluorescent intensity in the field is registered by a photomultiplier. The latter is a part of the workstation. X-ray irradiation knocks out an electron from an alkane molecule of the medium (these molecules are abundant). As a result, the primary pair of the solvent cation-radical and thermalized electron is produced, namely, $(Alk)^{+\bullet}/e^-$. In this system, a new ion-radical pair between $D^{+\bullet}$ and $A^{-\bullet}$ arises. The pair is initially formed in its singlet spin state and recombines producing electronically excited molecules. The latter are the objects to measure fluorescence intensity as a function of variable strength of the external magnetic field. Usually, one participant of $D^{+\bullet}/A^{-\bullet}$ pair is used in its perdeuterated form to be transparent for registration, whereas the other participant is looked out for. This allows registering the optically detected signal bearing information from only one of the counterparts. The sample solution is kept in the ambient temperature to quench (nonradiatively) triplet states, which are also formed during recombination. The method is sensitive to species with a very short time of living. Optically detected ESR methods are also applicable to follow transformation of ion-radicals prepared in conditions of pulse radiolysis. Thus, the cation-radical of 2,3-dimethyl-2-butene obtained during the pulse radiolysis of anthracene-d_{10} mixture with 2,3-dimethyl-2-butene shows in MARY spectra not four, but eight equivalent methyl groups. This result testifies for the formation of sandwich dimer, according to Scheme 4.27 (Desrosiers and Trufunac 1986).

4.4.1.2 Nuclear Magnetic Resonance Methods

The nuclear magnetic resonance (NMR) methods ascertain the concentration of ion-radicals and sometimes establish their structure. The concentration of ion-radicals in solution is determined either directly by the intensity of ion-radical signals or indirectly by splitting of the standard signal (Malykhin et al. 1975). Sometimes, a chemical shift of the solvent signal is observed in the presence of ion-radical (Screttas and Micha-Screttas 1982, 1983, Micha-Screttas et al. 2001). It is important, then, to understand the mechanism by which a solvent receives spin density. A pertinent example is the interaction of sodium fluorenone anion-radical, $(C_6H_4)_2C^{\bullet}$—ONa, as a paramagnetic species with HMPTA, that is, $(Me_2N)_3P \rightarrow O$, as a solvent (Screttas et al. 1998 and references therein). The mutual complex can be written as $(C_6H_4)_2C^{\bullet}$—ONa $\cdots$ O $\leftarrow$ $P(NMe_2)_3$. Usually spin density is transferred through covalent bonds. In the case considered, the phosphorus atom of HMPTA, though located a bond away from the paramagnetic center, still receives some spin density. Scheme 4.28 transmits the structure of the tetrameric sodium fluorenone anion-radical complex with HMPTA.

The complex possesses a Na_4O_4 cubic core in which each ketyl oxygen is bonded to three sodium atoms and each sodium to three ketyl oxygen atoms. The fourth coordination site on the metal is occupied by HMPTA ligand. So the metal can receive some spin density from the ketyl oxygen and transfer a part of this density to the phosphorus-containing ligand. This changes the solvent ^{31}P NMR pattern.



SCHEME 4.28

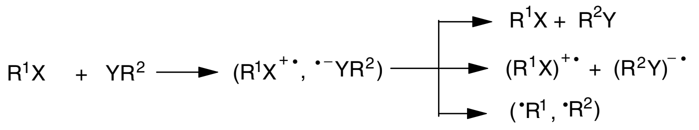
In this connection, attention should be paid to an unusual NMR technique called nuclear magnetic relaxation dispersion (NMRD). In contrast with NMR spectroscopy, the NMRD signal arises from the nuclei of the abundant solvent molecules and not from the dissolved substances. The relaxation properties of the solvent molecules are profoundly modified if the solvent contains paramagnetic particles (see a review by Desreux 2005). A solvent molecule sails in the vicinity of an ion-radical and finds itself in the local magnetic field of this paramagnetic particle. Then, induced magnetism of the solvent molecule dissipates in the solvent bulk. This kind of relaxation seems to be registered by NMR. NMRD is applicable to studies on ion-radical solvation/desolvation, ion-pair dynamics, kinetics of ion-radical accumulation/consumption, and so on.

A very important variety of NMR method deals with the detection of chemically induced dynamic nuclear polarization (CIDNP). CIDNP is far more sensitive than ESR with regard to detection of ion-radical stages of reactions. Particles with uniformly populated Zeeman levels give normal NMR spectra. Molecules produced as a result of radical–radical recombination may have nonuniformly populated Zeeman levels. This leads to abnormal NMR behavior called CIDNP—enhanced absorption at positive polarization and emission at negative polarization. The CIDNP signals are observed immediately after particle formation within the period of time necessary for nuclear relaxation. This time is 1–30 s. The NMR spectra often visualize the multiplet effect. The effect is observed when the lines in spin multiplet in high and low fields have opposite signs, revealing both emission and absorption.

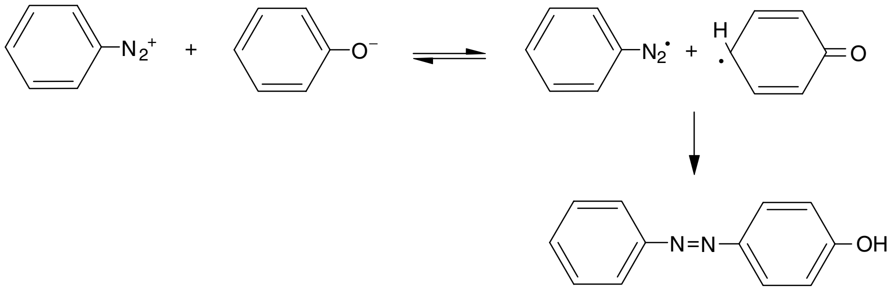
The CIDNP method proves that the reaction proceeds through intermediate paramagnetic particles (ion-radicals, radicals, biradicals, etc.). A pair of any spin carriers is a multispin system with manifold spin states. Chemical reaction selects those, which are spin-allowed. Any radical pair ($R^•$, $R^•$) needs to undergo triplet–singlet spin conversion to recombine and produce zero-spin diamagnetic molecule R–R. Thus, chemical reaction leaves spin-forbidden states unbound. These forbidden states undergo magnetically induced spin conversion. Therefore, any multispin pair is a spin-selective microreactor and potential source of magnetic effects. The CIDNP method establishes which radical pair gives rise to a molecule and determines the spin multiplicity of the reacting particles forming a radical pair. And CIDNP evaluates (by the kinetics of nuclear polarization) the rate constants of ion-radical conversions and their activation energies.

As with any other physical methods, the CIDNP method is not universal and not immune to misinterpretation. It has certain drawbacks: The polarization is weak and hardly detected in reactions involving extremely short-lived radicals and, if so, the polarization disappears quickly. It is often difficult to attribute the polarization to products of the main conversion, rather than the side or reverse conversions. The latter threat is most serious for the reactions with participation of ion-radicals—the formation of end products often proceeds concurrently with the restoration of the initial neutral molecules, due to a reverse electron transfer as in Scheme 4.29.

Scheme 4.29 shows that not only the end products but also the initial molecules can be polarized. Besides, one of the ion-radicals formed can exchange electrons with the neutral starting molecule. These phenomena and others, which can be attributed to electron exchange, lead to a loss



SCHEME 4.29



SCHEME 4.30

of memory in nuclear-spin states. In addition, the initial polarization may be scattered as a result of a chain ion-radical process (Chanon and Tobe 1982):

$$R^1Li + R^2X \rightarrow (R^1Li)^{+\bullet} + (R^2X)^{-\bullet}$$

$$(R^1Li)^{+\bullet} \rightarrow {}^\bullet R^1 + Li^+;\ (R^2X)^{-\bullet} \rightarrow {}^\bullet R^2 + X^-$$

$${}^\bullet R^2 + R^1Li \rightarrow {}^-R^2 + (R^1Li)^{+\bullet};\ {}^\bullet R^1 + R^2X \rightarrow {}^+R^1 + (R^2X)^{-\bullet}$$

$${}^-R^2 + Li^+ \rightarrow R^2Li;\ {}^+R^1 + X^- \rightarrow R^1X$$

Buchachenko (1974) has advanced another theory. He based his reasoning on the absence of CIDNP signals for the reaction of *n*-butyl iodide with *t*-butyl lithium conducted in ether at −70°C. The metal cation and iodide quickly exchange under these conditions, but the C—C bond does not form. In contrast to Scheme 4.29, Buchachenko's theory assumes that the radicals produced form complexes with alkyl lithium associates. Alkyl lithium forms stable hexamers (two pyramids having a common base) and tetramers (tetrahedrons). These associates exist even in the gas phase and are revealed by mass spectroscopy. A radical bonded in such cluster produces a paramagnetic widening of NMR signals. This makes them nonobservable long before the end of the reaction. Therefore, in this case, the absence of CIDNP effect is caused by its masking.

Another word of caution may be in order. The spectra may visualize nuclear polarization of products due to polarization of initial substances. Bubnov et al. (1972) recorded ^{15}N-NMR spectra to investigate azo coupling of benzene diazonium tetrafluoroborate with sodium phenolate in methanol. Benzene diazonium was prepared from aniline-^{15}N and $H^{15}NO_2$. The spectrum demonstrated a strong polarization of signals from the azo dye just after mixing of the solutions of the diazo compound and phenol. The signal from the initial diazonium salt was also polarized. Bubnov et al. concluded that the azo dye is produced as represented in Scheme 4.30, and the nuclear polarization of the diazonium nitrogen was regarded as an evidence of the reversibility of the electron stage.

Such treatment of CIDNP results produced serious objections. Lippmaa et al. (1973), investigating the same reaction, revealed a strong ^{15}N, ^{13}C, and ^1H CIDNP effect. The ^{13}C nuclei in the phenoxyl part of the azo dye were not polarized. At the same time, polarization of ^{15}N nuclei of the azo bond and ^{13}C nuclei at positions 1 and 2 of the free-of-hydroxyl phenyl ring connected with

the diazo link was an exact replica of the polarization of the same nuclei in the diazonium salt. This led to the conclusion that the diazo component polarizes as a result of side reactions; it is the diazo component that brings the polarization to the azo dye. Thus, the CIDNP effect does not support the ion-radical mechanism presented in Scheme 4.30. Several explanations of the observed CIDNP effect have been proposed. One of them is discussed here because it seems to explain a whole range of interactions of diazonium salts with phenolates, an interaction that is accompanied by a pronounced polarization of nuclei.

The reaction of a diazo cation with phenolate yielding an azo dye may proceed through the formation of a diazo ether. Kekule and Hidegh (1870) concluded this. Zollinger (1958), considering this conclusion, proposed and explained the mechanism by which the diazo ethers convert into C-diazo compounds, that is, hydroxyazo dyes. The diazo ether preliminarily dissociates into phenolate and diazonium ions, that is, a two-stage intermolecular reaction takes place. The CIDNP effect suggests that the diazo ether may reversibly convert into a radical pair according to the following equilibrium:

$$ArN_2^+ + {}^-OPh \rightleftharpoons ArN{=}N{-}OPh \rightleftharpoons ArN{=}N^\bullet, {}^\bullet OPh$$

While interacting with alkoxyl anions, the diazonium cation also produces primary diazo ether although it gives no azo dye. ^{15}N and ^{13}C nuclei of aryldiazonium tetrafluoroborate enriched with ^{15}N in both nitrogen positions become polarized in the presence of sodium alcoholates (Levit et al. 1971). The reaction yields benzene showing nuclear polarization. The data on kinetics and CIDNP results (Lewis and Chalmers 1971, Levit et al. 1972) agree well with the following sequence:

$$ArN_2^+ + {}^-OR \rightleftharpoons ArN{=}NOR \rightleftharpoons ArN{=}N^\bullet, {}^\bullet OR$$

$$ArN{=}N^\bullet \rightarrow N_2 + Ar^\bullet$$

$$Ar^\bullet + H(SolH) \rightarrow ArH$$

Schemes on interactions between arylazo cations and phenolates or alkoxyls have much in common. There is a very clear reason to consider them together.

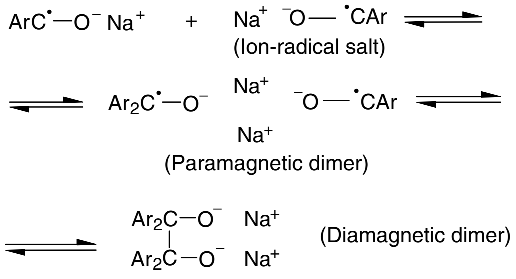
As discussed earlier, CIDNP method is of great help to chemists. However, it cannot always give straightforward information, because the CIDNP effect may be masked and errors may creep into its interpretation. CIDNP requires strong chemical and physical professional skills (which are useful for all the method considered here). However, using CIDNP, a researcher can be compensated by the reliability of the conclusions.

4.4.2 Optical Spectroscopy Methods

4.4.2.1 Electron Spectroscopy

Ion-radicals have, as a rule, a deeper coloring than the initial neutral molecules. An unpaired electron on the MO increases the molecule polarizability and facilitates its excitation by light. This enhances the intensity of absorption and shifts it to the region of higher wavelengths. Therefore, ion-radicals are quite easily revealed via electron spectroscopy. This method is often applied to investigate the ion-radical reaction kinetics and establish the significance of ion-radical pathway.

Of course, high reactivity of ion-radicals dictates some complexity in the registration methods, such as stop-flow spectroscopy or isolation of ion-radicals by capillary electrophoresis. Whereas stop-flow spectroscopy is used more or less frequently, capillary electrophoresis has been involved only in recent times. Choosing the appropriate capillary length, a researcher can isolate and register UV spectra of relatively less-stable ion-radicals. When the interaction of the corresponding



SCHEME 4.31

ion-radical with some reactant is an aim of the study, changes in UV spectra are accompanied with measurable decreases in electrophoretic mobility. For instance, electrophoretic analysis was successfully used in studies on phenanthrenequinone anion-radical and its H-bond complex with carbamide (Esaka et al. 2003).

Electron spectroscopy is also applicable to structural investigations of ion-radicals. There is an extensive body of works studying this matter. Spectrophotometry is indispensable in those cases where an equilibrium exists between the paramagnetic and diamagnetic forms of an ion-radical salt. For instance, ketyl dimers can be paramagnetic and diamagnetic. The dimers of sodium ketyls of fluorenone or benzoquinone are, in the main, paramagnetic ones in ether solvents. In hydrocarbon solvents such as toluene or cyclohexane, a portion of the paramagnetic species becomes smaller and color intensity changes to decrease markedly. Spectrophotometry fixes such a change clearly (Rao et al. 1972). The drop in absorptivity is a consequence of the formation of the diamagnetic dimer (Scheme 4.31).

Dimerization shown in Scheme 4.31 is reversible at all the steps. Both electron spectrometry and electron spin resonance are applicable to study the equilibrium, but the first method provides more accuracy.

It is interesting to compare electron spectroscopy and electron spin resonance with respect to substituent effects on electron systems of organic ion-radicals. The nitrobenzene anion-radical has a characteristic band in its UV spectrum at 440 nm. The band position is not changed markedly in the presence of electron donor substituents (OMe, NR_2) in the para position of nitrobenzene anion-radical. Electron acceptor groups (*p*-NO_2, *p*-CN, *p*-COMe) cause a very strong shift of the band toward larger wavelengths. Analogous effects are characteristic for anion-radicals of pyridine and azobenzene (Rao et al. 1972). In UV spectra, consequently, the influence of electron-donor substituents is practically imperceptible, whereas electron-acceptor substituents cause strong bathochromic shifts. ESR spectra, however, fix the influence of both the substituent types—in anion-radicals of nitrophenyl derivatives, donor substituents increase values of HFC constants of the nitro group at the nitrogen atom. In contrast, acceptor substituents diminish these constants (Todres 1981).

Acceptor substituents in nitrophenyl anion-radical frequently form quinoid structures. Donor substituents cannot participate in the formation of such structures. As to electron spectroscopy, it is very sensitive to changes in the electron structure of a chromophore system. The influence of acceptor groups is, therefore, stronger than that of donor groups. If changes in chromophore systems are absent, the method of spectrophotometry remains relatively less informative.

Methods of electron spectroscopy are widely used to follow the electron-transfer process. Thus, the progress of electron transfer from naphthalene anion-radical to cup-stacked carbon nanotubes is easily detected by monitoring the UV absorption spectrum. Namely, the absorption band around 500–900 nm due to naphthalene anion-radical completely disappears after reduction of the nanotubes. At the same time, the reduced nanotubes exhibit ESR spectrum characterized with *g*-factor of 2.0025 (Saito et al. 2006). This *g*-value is close to the free spin *g*-factor of 2.0023 that is diagnostic of the delocalized electron on carbon nanomaterials (Stinchcombe et al. 1993). It should be parallelly

noted that as a result of electron transfer, the stacked structure of the pristine nanotubes with mean size >6000 nm are disassembled to produce individual cup-stacked carbons with the controlled size of ca. 60 nm (Saito et al. 2006). For the applications of carbon nanotubes in integrated devices, minimization and control of the nanoparticle size are crucial (see, e.g., Hata et al. 2004).

4.4.2.2 Vibration Spectroscopy

When the solvents used are not masking the bands of ion-radical particles and particles are stable, the IR spectroscopy can also be employed. It gives some advantage in identifying the ion-radical structure (by a change in the number of absorption bands in ion-radical spectra or different pattern of the band distribution as compared to the initial neutral molecule). Moreover, vibration spectroscopy can determine the localization of spin density, that is, it can answer the key question concerning the structure of ion-radicals. For example, IR spectra of metalloporphyrine cation-radicals establish that spin density and positive charge are localized not on the metal (iron) but on the porphyrine ligand (Shinomura et al. 1981).

Vibration spectroscopy also measures the concentration of ion-radicals (through estimation of the band intensities). Moreover, the IR intensities of some bands in the fingerprint region for organic ion-radicals may be much larger than the intensities of the bands for the neutral parent molecules. The examples are anion-radicals of biphenyl and naphthalene. The positions and intensities of bands in their IR spectra were precisely measured using the technique of optical fibers. For precision, the anion-radicals were prepared in THF-d_8, a spectral glass-tube cell of an apt construction was connected to a reaction vessel within the line sealed in vacuum (Sakamoto et al. 2005). The vibration patterns of the intensity-carrying modes are analyzed and compared with the DFT calculated data.

Generally, vibration patterns are closely related to the electronic structure of ion-radicals (see also Torii et al. 1999 and references therein). In this sense, attention should be drawn to the nature of the parent molecule whose ion-radical is under IR investigation. Chloranil is a relevant example. In this neutral quinone, the highest frequency mode is the symmetric C=O stretching and second one is C=C stretching. In chloranil anion-radical (in *p*-semiquinone), strong mixing takes place due to the larger ionization shift of C=O stretch. Accordingly, the IR intensity of C=C stretch is drastically (2 order of magnitude) decreased on one-electron addition to chloranil (Ranzieri et al. 2007).

4.4.3 Other Physical Methods

4.4.3.1 Magnetic Susceptibility

Magnetic susceptibility of paramagnetic particles is used to determine the concentration of ion-radicals but yields no structural information. The method often demands solid samples of ion-radical salts. Many ion-radical salts are unstable in the solid state, and this requirement turns out to be a decisive limit. Fortunately, there are special ways to determine magnetic susceptibility of paramagnetic particles in solutions (Selwood 1958). However, instruments for such measurements are rarely used in chemical laboratories. Besides, special devices should be used to conduct investigations at different temperatures.

4.4.3.2 Mass Spectrometry

The behavior of ion-radicals in the mass spectrometer chamber opens up principal venues of their alteration. However, liquid-phase reactions (typical for ion-radical organic chemistry) have many peculiarities and mass-spectrometry methods of ion-radical transformations are not inevitably reproducible. This is quite evident and needs no further comments.

4.4.3.3 Electrochemical Modeling of Ion-Radical Reactions

By traditional understanding, electrochemistry is a science that considers transformations caused by an electrochemical reaction strictly, that is, by electrode depolarization. Organic depolarizers are

involved in electron transfer that, however, can be caused not only by the electrode discharge but also by simple interactions between donors and acceptors in a pool, that is, by pure chemical reactions. Contemporary organic electrochemistry is widening its scope everyday. Accordingly, more attempts appear to perform electrochemical modeling of ion-radical organic reactions. The differences and similarities between pure chemical and electrochemical (electrode) methods for studying ion-radical transformations were analyzed in Section 2.4. Therefore, we can directly enumerate requirements for accuracy in electrochemical modeling of organic ion-radical reactions.

The following approach is recommended:

1. By electrochemical and ESR methods, establish the behavior of every reaction participant and ascertain the sequence of its transformation, up to formation of a stable final product.
2. Determine the potentials of reversible one-electron waves for each participant. Comparing the potentials, estimate the probability of the whole ion-radical route for the reaction studied.
3. On the basis of data obtained, make an electrochemical model—use an electrode instead of a donor or an acceptor and employ solutions containing a supporting electrolyte, another reactant (an acceptor or a donor, correspondingly), and stable products, which this reactant produces as a result of ion-radical reaction.
4. Draw an analogy between chemical and electrochemical reactions. Such analogy is correct (i) if the principal intermediary and final products of the chemical and electrochemical reactions are identical; (ii) if a specific interaction of particles with an electrode material is absent; and (iii) if both systems (chemical and electrochemical) respond equally to changes of process conditions.

Concerning experimental feature of electrode processes, a newly developed specificity deserves to be mentioned. For *in situ* generation of ion-radicals by electrolysis, metal (most commonly, platinum) electrodes are used. Latest development of electrochemical methods has brought attractive characteristics of conductive boron-doped diamond electrodes. Among these characteristics, the most important problem is the very little tendency to foil by organic substrates during generating catalytic currents, which can often occur on metal electrodes. For instance, the boron-doped diamond electrode is used for generation of ascorbic acid anion-radical in nonaqueous electrolyte (Yoshimura et al. 2002).

Obviously, the heterogeneous character of electrochemical process can in some cases lead to essential differences between electrode and homogeneous reaction pathways. Therefore, eventually it needs to verify the results by studying of reactions in homogeneous media. In other words, the problem of correctness of electrochemical modeling should be analyzed for each reaction anew and at the same time be checked chemically, that is, in the pure liquid-phase conditions.

4.4.3.4 X-Ray Diffraction

It is well known that crystal and electronic structures are interdependent and define the reactivity of chemical substances. In Section 1.4.2, it was noted that copper–porphyrin complex gives cation-radicals with significant reactivity at the molecular periphery. This reactivity appears to be that of nucleophilic attack on this cation-radical, which belongs to π-type. The literature sources note, however, some differences in the reactivity of individual positions. A frequently observed feature in these π-cation derivatives is the appearance of an alternating bond distance pattern in the inner ring of porphyrin consistent with a localized structure rather than the delocalized structure usually ascribed to cation-radical. A pseudo Jahn–Teller distortion has been named as a possible cause of this alternation, and it was revealed by X-ray diffraction method (Scheidt 2001).

4.5 EXAMPLES OF COMPLEX APPROACHES TO DISCERNMENT OF ION-RADICAL MECHANISM OF ORGANIC REACTIONS

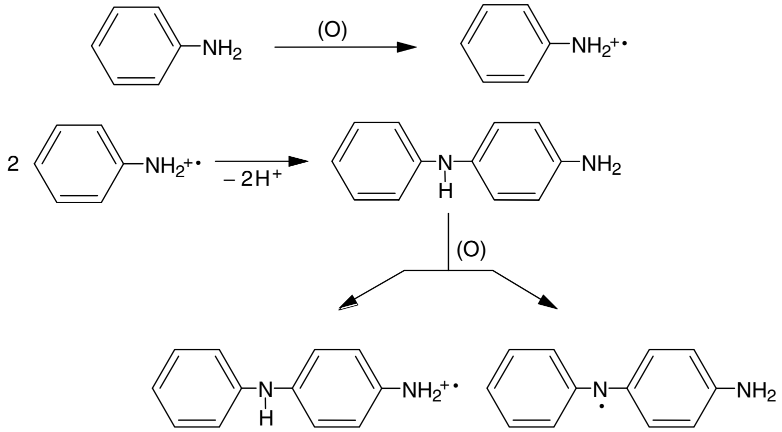
4.5.1 Oxidative Polymerization of Anilines

As a conducting polymer, polyaniline has many electronic-related applications such as rechargeable batteries (Tsutsumi et al. 1995), multilayer heterostructure light-emitting diode devices (Onoda and Yoshino 1995), biosensors (Bartlett and Whitaker 1987), electrochromic windows (Nguyen and Dao 1989), and nonlinear optical materials (Papacostadinou and Theophilou 1991). Recently, strong attention is directed to polyanilines confined in mesoporous silicon (Urbach et al. 2007 and references therein). The composite differs in almost perfect ohm contacts and can serve as outstanding silicon-based light-emitting devices and sensors. Polyaniline can be prepared from aniline by both electrochemical and chemical methods. The chemical method is considered more useful for mass production than electrochemical method.

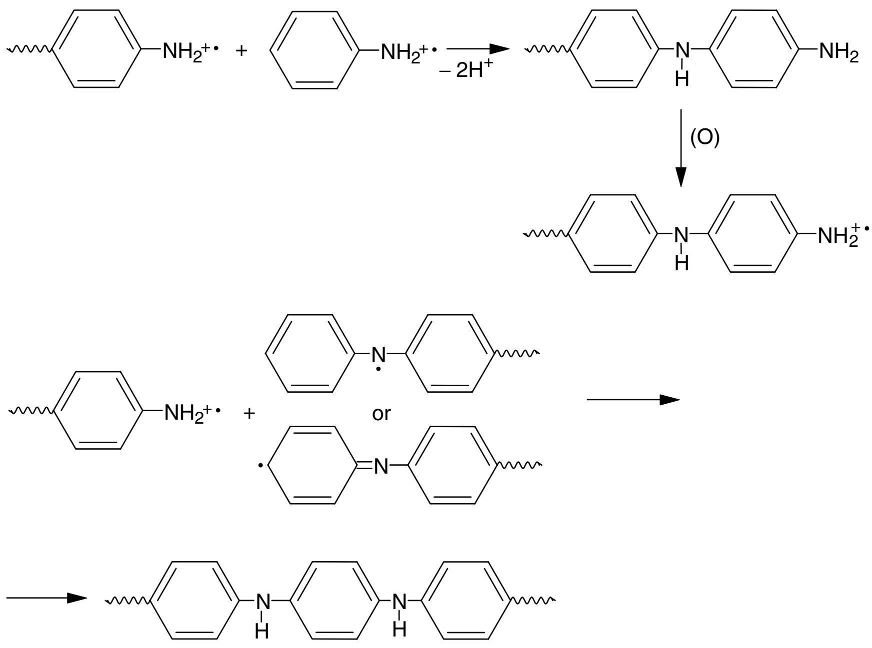
Although polyaniline synthesis has gained commercial importance, its polymerization mechanism is a subject of debate. Wei et al. (1989, 1990) as well as Ding et al. (1999) carried out oxidative polymerization of aniline in aqueous acidic solutions adding ammonium persulfate at 0°C and trapping agents. Ding et al. (1999) used a variety of organic compounds as traps. For instance, hindered phenols and electron-rich alkenes inhibited the polymerization, being traps for cation-radicals. All of the results obtained led to cation-radical polymerization mechanism of aniline, in which the polymerization is a chain-growth reaction through the combination of a polymeric cation-radical and aniline cation-radical. This mechanism mainly resembles the one discussed by Percec and Hill (1996). The formation of aniline cation-radicals and their dimerization are the initial steps of polymerization (Scheme 4.32).

The attack of monomeric cation-radical of aniline on oligomeric amine cation-radical leads to chain growth. The chain growth can also proceed as copolymerization of two oligomeric species (Scheme 4.33).

Scheme 4.33 presupposes the presence of $-NH_2^{+\bullet}$ groups in polyaniline. The presence of these groups was established during IR study on poly(3,5-dimethyl aniline) synthesized by using 3,5-dimethyl aniline as a monomer and palladium acetate as an oxidant (Mallick et al. 2005). Namely, the polymer displayed three peaks at 1300, 1325, and 1375 cm^{-1}, respectively. Such peaks correspond to $C–N^{+\bullet}$ stretching modes of the delocalizing polaronic charge carriers (Tagowska et al. 2004). The high intensity of the peaks indicated the richness of poly(3,5-dimethyl aniline) sample in these charge-carrier species.



SCHEME 4.32



SCHEME 4.33

Importantly, deep oxidation of polyaniline leads to a material that becomes insulating and spinless. This phenomenon was demonstrated in case of poly(*N*-methylaniline) by monitoring ESR signal and electric conductivity of the sample (Wei et al. 2007). Deep oxidation results in the formation of the so-called polaron pairs that are evidenced by optical spectra. Because the hopping probability of two polarons on a single chain is too small, polaron pairs do not contribute to electric conductivity and ESR signal.

The polymer resulting from oxidation of 3,5-dimethyl aniline with palladium was also studied by transmission electron microscopy (Mallick et al. 2005). As it turned out, the polymer was formed in nanofibers. During oxidative polymerization, palladium ions were reduced and formed palladium metal. The generated metal was uniformly dispersed between the polymer nanofibers as nanoparticles of 2 mm size. So, Mallick et al. (2005) achieved a polymer- metal intimate composite material. This work should be juxtaposed to an observation by Newman and Blanchard (2006) that reaction between 4-aminophenol and hydrogen tetrachloroaurate leads to polyaniline (bearing hydroxyl groups) and metallic gold as nanoparticles. Such metal nanoparticles can well be of importance in the field of sensors, catalysis, and electronics with improved performance.

4.5.2 Reactions of Hydroperoxides with Phosphites and Sulfides

It is well known that phosphites or sulfides added to stabilizers of polymeric materials considerably enhance the stabilizing effects. Destruction of polymers is caused by the action of peroxides resulting from oxidation at the defects of polymeric chains. The additives decompose hydroperoxides according to the following equations:

$$R^1{-}OOH + (R^2O)_3P \rightarrow (R^2O)_3P{=}O + R^1{-}OH$$

$$R^1{-}OOH + R^2R^3S \rightarrow R^2R^3S{=}O + R^1{-}OH$$

While investigating the mechanism, Pobedimskii and Buchachenko (1968a, 1968b) concluded that these reactions have an ion-radical nature and consist of electron transfer from phosphites or sulfides (denoted further as D) to hydroperoxides as follows:

$$R^1{-}OOH + D \rightarrow [(R^1{-}OOH)^{-\bullet}; D^{+\bullet}] \rightarrow [R^1{-}O^\bullet, {}^-OH, D^{+\bullet}]$$

As noted, the products of electron transfer retained in the solvent cage. Benzene was used as a solvent in these experiments. The cage complex $[R^1{-}O^\bullet, {}^-OH, D^{+\bullet}]$ decays either on disproportionation in the cage or dissociation. Disproportionaton leads to phosphinoxides or sulfoxides mentioned earlier. Dissociation results in the passage of radicals out of the cage into the solvent pool.

To check the possibility of primary electron transfer, hydroperoxides were allowed to react with the donors contained the stabilizing groups, namely, 4,4′-di(anisyl) sulfide or 1,2-dihydroxyphenyl-bis[2,4,6-tri(*tert*-butyl)phenyl]phosphite. The ESR method revealed formation of corresponding cation-radicals. The radical trap 2,2,6,6-tetramethylpiperidine-1-oxyl ($RNO^\bullet$) decayed when introduced into the reaction mixture. The rate of $RNO^\bullet$ decay was determined by ESR spectroscopy, whereas the rate of ROOH consumption in the reaction with an additive was discovered through polarography (by evaluating the residual part of ROOH). The rate constants of both processes were proven to be practically the same. According to the authors, the $RNO^\bullet$ decay proceeds only at the expense of ion-radical reaction. (It is worthwhile noting, however, that another trap, 5,5-dimethyl-2-phenyl-1-pyrroline *N*-oxide, reacts in benzene with perbenzoic or perpropionic acids to produce significant amount of aminoxy radicals as a result of addition of a peracid to the trap [Sang et al. 1996].) In the papers by Pobedimskii and Buchachenko (1968a, 1968b), the kinetics of decay fully corresponds to the kinetics of bimolecular reaction (ROOH + D). The radicals formed are extremely active and rate of $RNO^\bullet$ consumption is almost independent of its concentration in solution. In the presence of oxygen, however, the rate of $RNO^\bullet$ consumption markedly decreases (when $[O_2]_0 >> [RNO^\bullet]_0$). This is explained by the fact that oxygen converts a significant amount of active radicals into peroxide radicals, which do not react with $RNO^\bullet$. The rate of hydroperoxide consumption is independent of whether the foreign radical $RNO^\bullet$ is introduced into the system or not. Hence, the reaction is not a chain reaction. When the reaction is conducted in alcohol diluted with $H_2{}^{18}O$, the donor (phosphite) and hydroperoxide produce phosphate and alcohol not bearing the label. This means that the reaction considered either does not produce free ions ^-OH or does not exchange them with the medium. According to ion-radical equation, the isotope exchange should not take place if the ion-radical complex monomolecularly disproportionates. The rate constant of disproportionation is independent of the solvent viscosity, whereas the rate constant of $RNO^\bullet$ consumption decreases as the viscosity of the medium rises. This decrease corresponds to the Stokes–Einstein law. This is typical for the reactions occurring in the solvent cage.

The next step was to replace benzene as a solvent by styrene or methylmethacrylate. The mentioned solvents contain the ethylenic bond, which is attractive for the radicals. This generates a driving force for the radicals to leave the solvent cage. The general rate of the process in vinyl-containing solvents remains the same as that in benzene, whereas the rate of $RNO^\bullet$ consumption increases. Naturally, more radicals leave the cage and pass into the pool due to their affinity for solvent molecules. So the inference follows that the reaction proceeds by a radical mechanism. However, the amount of radicals leaving the cage is small because they disproportionate inside the cage at such a high rate that even the rate of radical addition to the ethylenic bond cannot compete with it.

This inference is checked stereochemically. If hydroperoxide produces alcohol at the expense of disproportionation of radicals not leaving the cage, the enantiomeric hydroperoxide should give alcohol that retains its optical activity. And this is what actually takes place (Davies and Feld 1958).

The material considered here allows us to understand the influence of sterically hindered amines, which act as stabilizers against the light-induced degradation of polyolefines. The sterically hindered amines easily undergo oxidation after cation-radical formation:

$$ROO^\bullet + {>}NH \rightarrow [ROO^- + {>}NH^{+\bullet}] \rightarrow ROOH + {>}N^\bullet$$

This equation seems to be a key reaction point in the antioxidant action of these amines—>N• radicals in the presence of oxygen are transformed via peroxy radical intermediates into nitroxyl radicals. The nitroxyl radicals are very persistent and react efficiently with radicals produced on polyolefine degradation. Such radical interception blocks the chain in radical oxidation and therefore causes the antioxidant activity of sterically hindered amines (Brede et al. 1998).

4.5.3 TER MEER REACTION

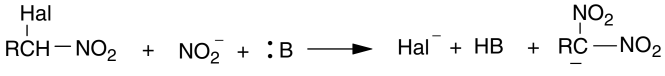
The ter Meer reaction consists of the production of 1,1-dinitro compounds from 1-halo-1-nitroalkanes. The reaction proceeds under the action of alkali metal nitrites in basic medium (Scheme 4.34).

The reaction of Scheme 4.34 is used to synthesize 1,1-dinitroalkanes, which find wide application as intermediate products in preparing drugs, biologically active substances, and high-energy compositions.

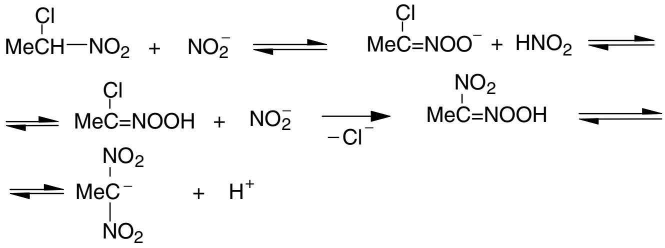
It was established several decades ago that the reaction of 1-chloro-1-nitroethane with sodium nitrite in aqueous alcohol is second-order overall and first-order in each reactant (Hawthorne 1956). 1-Deutero-1-chloro-1-nitroethane reacts more slowly than its lighter isotopomer. This means that the kinetic isotope effect is observed. The reaction proceeds only in moderately alkaline media; in strongly alkaline media, it does not take place. Only those geminal halo nitro compounds, which carry hydrogen in the geminal position, can undergo the conversion. On the basis of these facts, Hawthorne (1956) suggested S_N2 substitution preceded by isomerization of the initial substrate into aci-nitro form according to Scheme 4.35.

Recent research into the ter Meer reaction (Shugalei and Tselinskii 1994) has demonstrated that it actually chooses the chain ion-radical mechanism. Chain branching is attributed to air oxygen, after transformation into the superoxide ion ($O_2^{-\bullet}$; see Section 1.7.1). The whole process of substitution in the aqueous-alkaline buffer medium is expressed by a 14-step sequence summed in Scheme 4.36.

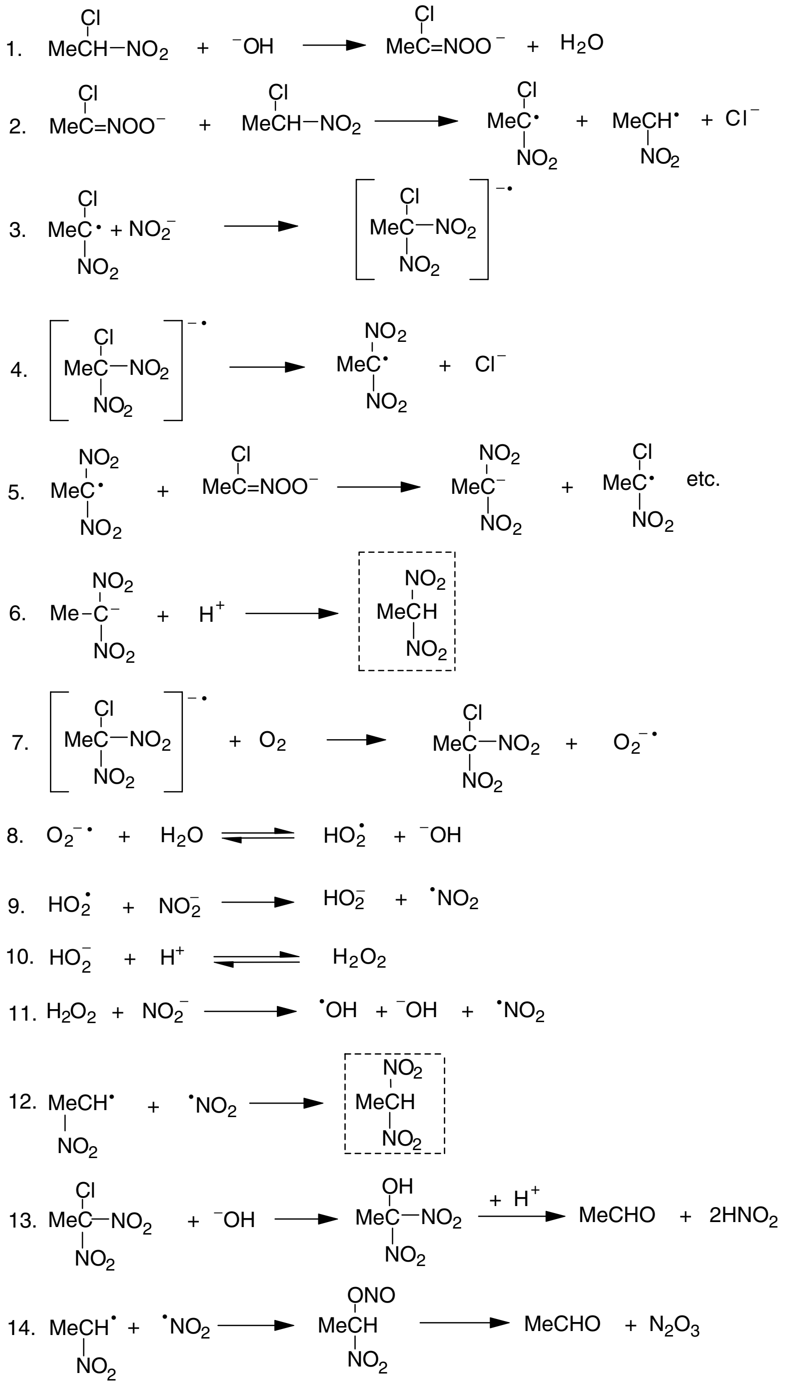
The 14-step sequence in Scheme 4.36 takes into account the data obtained by Hawthorne (1956) and accords well with later results. The mechanism depicted has been supported as follows. In a moderately alkaline medium, the substrate ionization at stage 1 completely governs the kinetics of the reaction (Shugalei et al. 1978). This agrees with the kinetic isotope effect and essential presence of hydrogen atom in the geminal node. For a chain ion-radical process to originate at stage 2, the reaction mixture should contain both the neutral substrate and corresponding anion. This explains why ter Meer reaction does not occur with excess alkali. All the initial molecules convert into anions, and electron exchange becomes impossible because there is no neutral substrate—an acceptor of an electron—in the reaction mixture. It has been revealed that lack of alkali also decelerates the conversion. In the acetate-buffer solution, the rate of the process drops and kinetic characteristics cease to obey the chain process laws. Under these conditions, the reaction remains a radical one, and the



SCHEME 4.34



SCHEME 4.35



SCHEME 4.36

introduction of 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl ($R^{OH}NO^{\bullet}$) inhibits the conversion. The aci-nitro anion is required not only for the origin (stage 2) but also for the development of the chain process (stage 5).

The presence of halonitro compounds, which are incapable of producing carbanion (such as 2-chloro-2-nitropropane and trichloronitromethane), considerably increases the rate of chain

origin in an alkaline medium, pH >8.0. These compounds accept electrons instead of nonionized 1-chloro-1-nitroethane, the concentration of which is small at a high alkalinity.

The chain propagation (stage 3) involving the addition of 1-chloro-1-nitroethyl radical to nucleophilic nitrite ion has been supported by a number of works devoted to the radical interaction with anions (see, e.g., Chawla and Fessenden 1975). Stage 4 presupposes that the anion-radical of 1-chloro-1,1-dinitroethane is only slightly stable and decomposes into the radical and anion. This agrees with the results of the investigations of polarographic behavior of geminal halonitroalkanes conducted with the help of ESR spectroscopy (Shapiro et al. 1969). And finally, stage 5 of one-electron oxidation of aci-nitro anion by 1,1-dinitroethyl radical is a well-known process. It regenerates the main particle, chloronitroethyl radical, which acts as an initial species for a new chain.

In a moderately alkaline medium, the ter Meer reaction proceeds through a considerable induction period; the kinetic curves are S-shaped. Peroxide compounds and UV irradiation accelerate the process (Bazanov et al. 1978). Radical traps inhibit the reaction (as discussed earlier). This indicates the radical nature of the process. The rate of formation of active radical centers obeys the second-order equation in the total concentration of chloronitroethane introduced into the reaction. In nonionized substrate and anion conjugated with it, the reaction is a first-order one. The rate of the whole reaction is independent of the nitrite concentration.

The superoxide ion or its protonated form (hydroperoxy radical $HO_2^{\bullet}$) is produced in the system (Shugalei and Tselinskii 1993, 1994). Hydroquinone, which is known to interact effectively with superoxide ion (Afanas'ev and Polozova 1978), exerts fairly strong inhibiting effect on the reaction. Addition of potassium ferricyanide to the system has, in contrast, an accelerating effect. The cause of the effect consists of transformation of the following type:

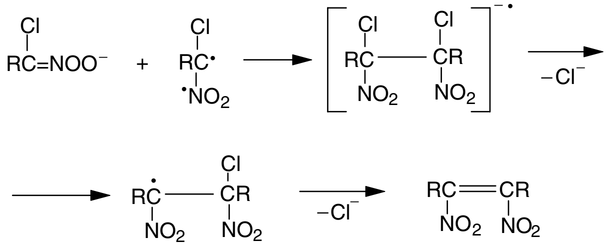
$$Fe^{3+\bullet} + HO_2^- \rightarrow Fe^{2+} + HO^{\bullet}$$

The chain ion-radical mechanism of ter Meer reaction has been supported by a thorough kinetic analysis. The reaction is well-described by a standard equation of chain-radical processes (with square-law chain termination) (Shugalei et al. 1981). This mechanism also explains the nature of side products—aldehydes (see steps 13 and 14) as well as vicinal dinitroethylenes. Scheme 4.37 explains formation of vic-dinitroethylenes.

The data on kinetics of parallel reactions permitted Shugalei et al. (1981) calculating the rate constants of competing pathways, which are essentially the constants of the conversion selectivity. The analysis of the constants allowed the authors to formulate the optimal conditions of ter Meer reaction's synthesis of 1,1-dinitroalkanes.

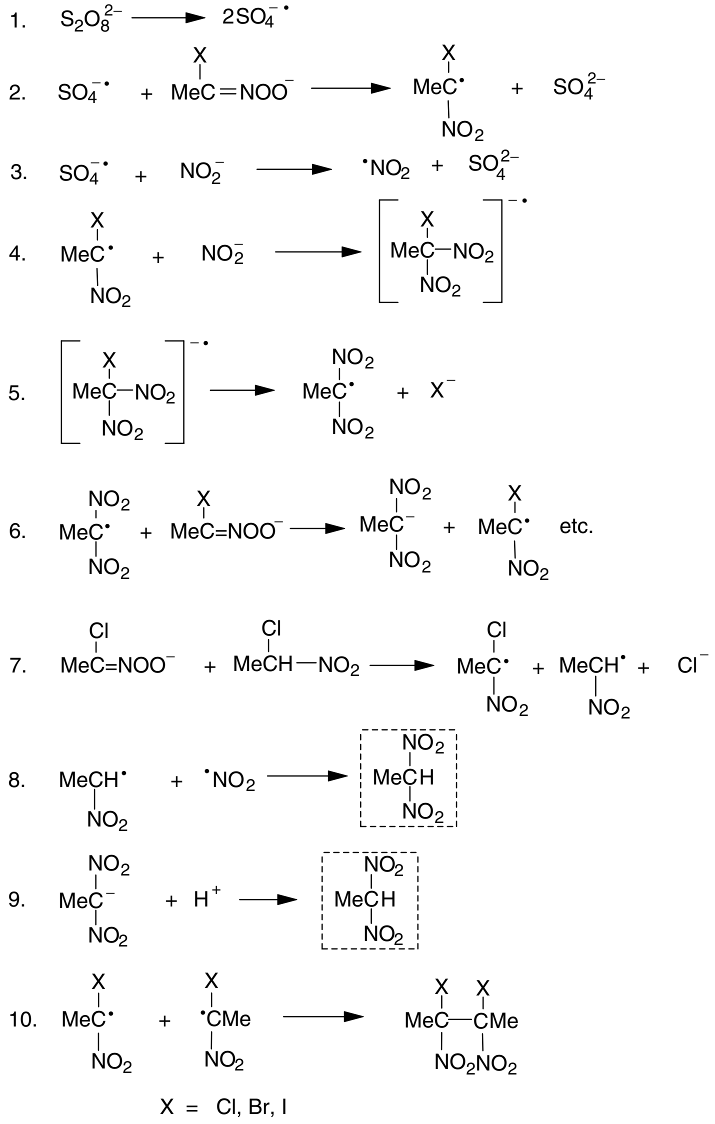
They suggested conducting the reaction at concentrations of the initial reagents, 1-halo-1-nitroalkane and sodium nitrite, exceeding 1 mol · L^{-1}. Then, because of the low solubility of molecular oxygen in water (approximately 10^{-4} mol · L^{-1}), the presence of oxygen does not affect the yield of the target product. An increase in the concentration of nitrite ion promotes ter Meer reaction.

Increasing the concentration of alkali up to a certain limit also accelerates the reaction; above this limit, however, alkali produces an adverse effect on the reaction. Therefore, the optimal

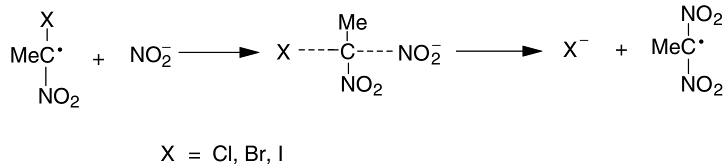


SCHEME 4.37

concentration of alkali should be determined in each particular case. Bazanov et al. (1980a, 1980b) suggested the following solution to this problem: They recommended the use of strongly alkaline medium and sodium persulfate. 1-Halo-1-nitroethane does not react with sodium nitrite in 0.01 N aqueous sodium hydroxides (the substrate converts into an anion entirely, and the system has no electron acceptor). The persulfate dianion performs the acceptor function, and 1,1-dinitroethane forms an 80–90% yield. As known (Pagano and Shechter 1970), the persulfate dianion oxidizes nitro carbanions to nitro alkyl radicals. The chain ion-radical nature of the reaction involving persulfate was proved with the help of the stable radical $R^{OH}NO^{\bullet}$ as described earlier. The rate of chain origin in the persulfate version of ter Meer reaction depends on the concentrations of halonitroethane, nitrite, and persulfate. Changing the concentration of hydroxide and removing molecular oxygen from the reaction mixture practically does not affect the rate of chain initiation. It has been established (Bazanov et al 1980a, 1980b, Shugalei et al. 1981) that the persulfate dianion initiates chains while oxidizing both aci-nitro anions and nitrite (see steps 1–10 of Scheme 4.38).



SCHEME 4.38



SCHEME 4.39

Step 2 represents the chain origin, step 3 is nitrite-ion oxidation, steps 4–6 are the chain propagation, and steps 8 and 10 show the chain termination at the expense of radical dimerization. Steps 4 and 5 can probably be united into one stage, as Scheme 4.38 points out.

The anion-radical of 1-halo-1,1-dinitroethane is not a kinetically independent particle because of its instability (Shapiro et al. 1969). Therefore, the addition of nitrite ion to halonitro alkyl radical and decomposition of the anion-radical of 1-halo-1,1-dinitroethane can proceed in a single stage as shown in Scheme 4.39. From Scheme 4.39, the effect of the leaving group—the halide ion—depends on the halogen's affinity to electron and energy of the cleavage of carbon–halogen bond. The difference between these two energies increases in the series of chlorine, bromine, and iodine derivatives (10, 14.7, and 60 $kJ \cdot mol^{-1}$, respectively). The coupling–cleaving merged scheme obviously demonstrates that 1-fluoro-1-nitroethane is incapable of participating in ter Meer reaction—the C–F bond in the anion-radicals of fluoronitro alkanes is extremely stable (Shapiro et al. 1969). This excludes the possibility of fluoride-ion elimination. The difference between the fluorine affinity to electron and energy of C–F bond disruption is $-127.5\ kJ \cdot mol^{-1}$ (Bazanov et al. 1980b).

The revealed mechanism of ter Meer reaction is well-founded. It helps us to understand the peculiarities of nucleophilic substitution reactions having the chain ion-radical mechanism and involving the interaction of radicals with anions at the chain propagation steps. It also demonstrates how the knowledge of kinetics and mechanism can be used to find new ways of initiating and optimizing the reactions important for technical practice. The ter Meer reaction turns out to be a reaction having one name and mechanism. This differs from, say, aromatic nitration, which has one name but different mechanisms.

4.5.4 Aromatic Nitration

In the past two decades, there has been an increasing recognition that ion-radicals play a very important role in many organic reactions. Eventually, a situation has arisen where, for practically every reaction between a donor and an acceptor, an ion-radical mechanism has to be carefully considered in addition to the classical polar pathway. The very subject of this book directs attention to cases where ion-radical formation is the obvious effect in play.

A substantial body of data concerning reaction kinetics, structure-reactivity relationships, and CIDNP have permitted a thorough understanding of electron-transfer steps in aromatic nitration. The following review materials can be addressed: Todres (1985), Morkovnik (1988), Ridd (1991, 1998), Eberson et al. (1994, 1995), Kochi (1990, 1992), Cardoso and Mesquita Carneiro de (2001), and some kind of bible—the monograph by Olah et al. (1989). Recent publications (Esteves et al. 2003, Gwaltney et al. 2003) from Olah's and Kochi's groups give a unified mechanistic concept of electrophilic aromatic nitration. In principle, the general mechanism of nitration includes the following distinct steps:

1. Generation of the electrophile: $2H_2SO_4 + HNO_3 = NO_2^+ + 2HSO_4^- + H_3O^+$ or $HNO_3 = NO_2^+ + NO_3^- + H_2O$.
2. Attack on the aromatic ring and formation a π-complex or electron donor–acceptor complex: $NO_2^+ + ArH \rightarrow ArH \cdots NO_2^+$. This complex involves high electrostatic and charge-transfer interactions between the π-aromatics and nitronium ion.

3. Formation of an intimate ([cation-radical]-radical) pair, $[ArH^{+\bullet}/^{\bullet}NO_2]$: This pair is, essentially, a single-electron transfer complex, indicative of one-electron oxidation of an aromatic compound by nitronium.
4. Collapse of the pair formed in step 3, to afford σ-complex: $[ArH^{+\bullet}/^{\bullet}NO_2] \rightarrow Ar^+(H)NO_2$.
5. Deprotonation of σ-complex: $Ar^+(H)NO_2 \rightarrow ArNO_2 + H^+$.

There are many testimonies for the cation-radical formation during electrophilic aromatic nitration. Positional selectivities are in line with spin-density distributions. In principle, the attack of $^{\bullet}NO_2$ radical is probably at the position of the aromatic cation-radical, which bears the maximal spin density.

For instance, nitration of naphthalene, azulene, biphenylene, and triphenylene proceeds preferentially in positions with the greatest constant of hyperfine splitting at the hydrogen atom in ESR spectra of corresponding cation-radicals. The constant is known to be proportional to the spin density on the carbon atom bearing the mentioned hydrogen. It is important, however, that the same orientation is also observed at classical mechanism of nitration in cases of naphthalene, azulene, and biphenylene, but not triphenylene (see Todres 1985).

According to calculations (Dewar et al. 1956), triphenylene itself has position 2 as the most reactive one for classical reactions. For its cation-radical, the most reactive position is at C-1, along with the same position 2 (Perrin 1977). These predictions and experiments are in line with triphenylene cation-radical participation in nitration (Baker et al. 1955).

For aromatic electrophilic substitution, positional selectivity is defined in terms of the ability of an atom in an aromatic ring to give the most stable bond on σ-complex formation. In the dibenzofuran case, calculations predict C-2 σ-complex to be more stable than C-3 σ-complex by 7.25 and 12.5 kJ for nitration and acetylation, respectively. Experimental data are in accordance with this estimation only for acetylation—$2 \gg 3 > 4 > 1$ (MeCOCl reagent, $AlCl_3$ catalyst, and CH_2Cl_2 solvent; at 0°C reaction temperature). As for nitration, position 3 turns out to be the most active—$3 \gg 2 > 1 > 4$ (99% HNO_3 and CH_2Cl_2, at −45°C). The preferential nitration in position 3 is seemingly not accidental. The maximal spin density is localized in just the same position of dibenzofuran cation-radical. The authors of the cited work conclude that acetylation follows the classical scheme, and the nitration proceeds through cation-radical formation (Keumi et al. 1988).

For the cation-radicals of benzenes bearing good leaving groups, calculations predict ipso addition of $^{\bullet}NO_2$ (De Queiros et al. 2006). Indeed, *tert*-butyl and trimethylsilyl substituents are changed by the nitro group as a result of the reaction of the corresponding benzene derivative with NO_2BF_4 in CH_2Cl_2 (Attina et al. 1996).

On one hand, there is a strong presumption against cation-radical mechanism of σ-complex formation (see Eberson et al. 1994). On the other, there is a strong correlation between selectivity in nitration and spin distribution in substrate cation-radicals. There were attempts (see, e.g., Morkovnik 1988) to reconcile such a contradiction by means of the following mechanism. The electron transfer is in fact an inner-sphere transfer, in the framework of a σ-complex. In this case, the energy restrictions are removed. The σ-complex gives a substrate cation-radical and $^{\bullet}NO_2$ radical. These species form a new complex (σ′), which is isomeric to the σ-complex with respect to the position of nitro group. The σ′-complex expels a proton and gives the final product:

$$NO_2^+ + ArH \rightarrow Ar(H)NO_2(\sigma\text{-complex}) \rightarrow {}^{\bullet}NO_2, ArH^{+\bullet} \rightarrow$$
$$\rightarrow Ar(H)NO_2(\sigma'\text{-complex}) \rightarrow ArNO_2 + H^+$$

This mechanism seems to imply that if some substitution occurs at the classical position of attack (the first σ-complex), then such a substitution should show the deuterium isotope effect for proton loss from this position. The deuterium effect is absent in the majority of nitration cases, except for nitration in sterically shielded positions (Schoffield 1980). Perhaps a systematic investigation of

kinetic isotope effects would be useful in a much wider range of substrates in comparison with their IPs and nitration conditions.

Feng et al. (1986) performed quantum-chemical calculations of aromatic nitration. The results they obtained were in good accordance with the IPs of $^{\bullet}NO_2$ and benzene and its derivatives. The radical-pair recombination mechanism is favored for nitration whenever the IP of an aromatic molecule is much less than that of $^{\bullet}NO_2$. According to calculations, nitration of toluene and xylene with NO_2^+ most probably proceeds according to ion-radical mechanism. Nitration of nitrobenzene and benzene derivatives with electron-acceptor substituents can proceed through the classical polar mechanism only. As for benzene, both mechanisms (ion-radical and polar) are possible. Substituents that raise the IP of an aromatic molecule to a value higher than that of $^{\bullet}NO_2$ prevent the formation of this radical pair (one-electron transfer appears to be forbidden). This forces the classical mechanism to take place. It should be underlined that a solvent plays the decisive role in nitration.

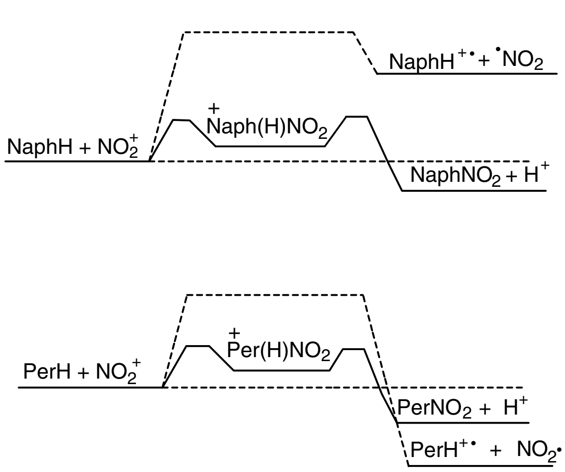
In comparison with gas-phase conditions, the calculated IP of $^{\bullet}NO_2$ in a solvent with a dielectric strength of 78.5 (as that in water) is reduced significantly. The diminution is stronger than that of either benzene or toluene (Feng et al. 1986). This is a consequence of the fact that NO_2^+ ion is preferentially stabilized in dielectric media. The nature of the solvent is, therefore, quite important for nitration reaction in the sense of which mechanism is operative.

Examples of multiplicity of nitration mechanisms that depend on IPs of substrates are the nitration of naphthalene (NaphH + NO_2^+ system) and perylene (PerH + NO_2^+ system) (Scheme 4.40).

In both NaphH + NO_2^+ and PerH + NO_2^+ systems, the transition state of heterolytic reaction lies energetically lower than the transition state of electron-transfer reaction. However, IP of perylene is significantly less than that of naphthalene. Therefore, $PerH^{+\bullet}$ cation-radical has lesser energy than $NaphH^{+\bullet}$ cation-radical. In other words, the products of reaction PerH + $NO_2^+ \rightarrow PerH^{+\bullet} + {}^{\bullet}NO_2$ find themselves in an energetically permitted zone (which is lower than that of the initial level). Meanwhile, the products of reaction NaphH + $NO_2^+ \rightarrow NaphH^{+\bullet} + {}^{\bullet}NO_2$ find themselves in an energetically forbidden zone (which is higher than that of the initial level).

Neutral perylene reacts with NO_2^+, giving the cation-radical. However, its formation is, in principle, a result of σ-complex splitting. Another possible route of σ-complex splitting consists of proton elimination and nitro perylene formation. As experiments show, the nitration of perylene is accompanied with collateral reactions of $PerH^{+\bullet}$, such as recombination and interaction with solvent molecules (Eberson and Radner 1985). This testifies to the release of cation-radical.

According to Scheme 4.40, $NaphH^{+\bullet}$ cation-radical cannot be formed as a result of interaction of NaphH with NO_2^+. In this sense, Ridd's work is relevant (see Johnston et al. 1989, 1991). The work shows that, to some extent, the nitration of naphthalene can indeed proceed through an outer-sphere

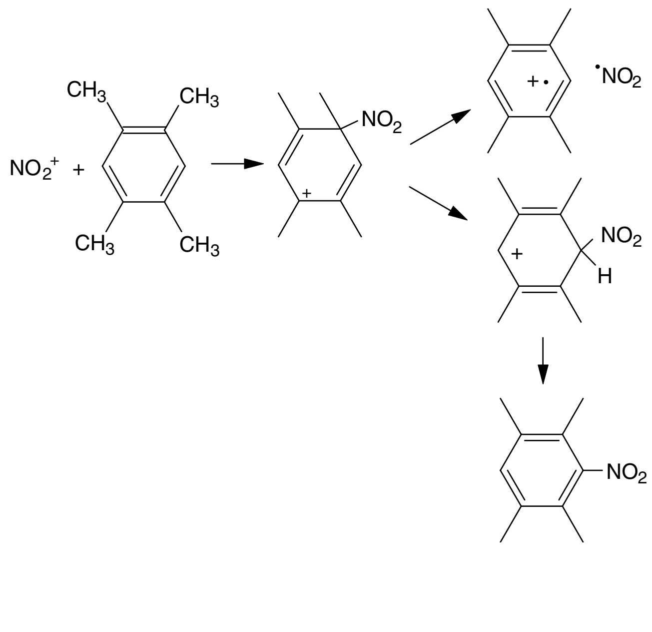


SCHEME 4.40

electron transfer. Naphthalene, durene, and mesitylene were compared in their reactions with $H^{15}NO_3$. The reactions were performed in a solvent containing trifluoroacetic acid (49%), nitromethane (50%), and water (1%) (weight to weight). The reaction mixture also contained some amount of sodium azide and methanesulphonic acid. Sodium azide was needed to stop the nitrous acid–catalyzed nitration (see later) and methanesulphonic acid was used to bring the reaction rate to the required value. The role of nitromethane deserves a special explanation. According to electrochemical data (Boughriet and Wartel 1989), log*K* for the reaction NaphH + NO_2^+ = $NaphH^{+\bullet}$ + $^{\bullet}NO_2$ has the following values in diverse solvents: −8.67 (AN), 0.8 (sulfolane), and 6.75 (nitromethane). These results imply that the boundary between classical and electron-transfer mechanisms of nitration is likely to be very dependent on the solvent used, with nitromethane favoring the electron-transfer process.

The aforementioned reaction was monitored by ^{15}N NMR. Under these conditions, nitromesitylene showed no effect of nuclear polarization. Nitronaphthalene was revealed slightly, but trustworthily enhanced absorption of ^{15}N signal. Because the conditions of nitration were strictly the same for both substrates, artifacts from the solvent or other components of the mixture were excluded. The observed enhanced absorption could not be caused by catalytic influence of HNO_2. When perdeuteronaphthalene was used as a substrate, the nitro product obtained gave no further enhancement of NMR absorption. The authors concluded that a small part (a few percent) of the reaction of naphthalene with nitronium ion does involve direct electron transfer between the reactants before the formation of σ-complex. Under the experimental conditions, an encounter or *π*-complex (a predecessor to σ-complex) is distinguished by such a strong interaction between its components that bending of the nitronium cation occurs at this very initial stage. Some rather small part of the encounter complex gives electron-transfer products, that is, naphthalene cation-radical and nitrogen dioxide. The latter form the polarized nitronaphthalene after recombination. Hence, one cannot "completely rule out some contribution from electron transfer in the nitration of naphthalene, particularly if the initial π-complex interaction is considered to be sufficient to treat the electron transfer as an inner-sphere reaction" (Ridd 1991).

The reaction of durene with $H^{15}NO_3$ under the conditions just mentioned is another specific but principally important case. The reaction is accompanied with a strong enhanced absorption in ^{15}N NMR spectrum with respect to a signal belonging to the product, that is, nitrodurene. Durene and naphthalene have very similar standard potentials (2.07 and 2.08 V, respectively, in AN; see Ridd 1991). A significant difference between them is that, with durene, much of the nitration supposedly arises from ipso attack followed by rearrangement according to Scheme 4.41.



SCHEME 4.41

The CIDNP studies show that a significant part of the overall reaction involves the corresponding durene cation-radical. "It is reasonable that the radical cation should be formed in the rearrangement stage rather than in the initial substitution, for different geometry of nitrogen dioxide (bent) and nitronium ion (linear) lead to high reorganization energy for electron transfer to the nitronium ion. Since O—N—O bond in the nitro group is bent, the change in geometry is less when nitrogen dioxide molecule is formed by homolysis of a C—NO_2 bond. Of course, the direct reaction (the first step of the preceding scheme) also involves a major change in the geometry of O—N—O group, but the energy terms involved in bond formation should then stabilize the transition state" (Ridd 1998).

When considering aromatic nitration, it seems reasonable to examine other nitrating agents (besides the nitrating mixture leading to the formation of nitronium ion) and outline the scope of ion-radical mechanism in each case.

4.5.4.1 System of HNO_3 and H_2SO_4 with Catalytic Amounts of HNO_2

A mixture of HNO_3 and H_2SO_4 is a classical tool for aromatic nitration. However, the presence of nitrous acid is sometimes necessary. For instance, naphthalene-1,3,5-trisulfonic acid gives 8-nitro-naphthalene-1,3,5-trisulfonic acid on reaction with a technical nitrating mixture. However, this starting trisulfonic acid remains unchanged if pure sulfuric acid and nitric acid free of nitrogen oxides are employed (Ufimtsev 1983). The addition of $NaNO_2$ is needed to nitrate naphthalene with nitric acid in sulfuric acid of 56% concentration (Ross et al. 1983). Nitrous acid has a catalytic effect on the nitration of activated aromatic compounds. The typical examples refer to aniline, *N*,*N*-dialkylanilines, phenols, anisole, and mesitylene (Brickman and Ridd 1965, Giffney and Ridd 1979, Gorelik et al. 1995). The role of nitrous acid was initially interpreted as nitration through nitrosation when nitric acid oxidized a primary formed nitroso compound. Such a mechanism is presently admitted for nitration of phenols and *N*,*N*-dialkyl aromatic amines. Thus, in nitrous acid–catalyzed nitration of anisole in 43–47% sulfuric acid (Dix and Moodie 1986), the intermediate *p*-nitrosoanisole undergoes demethylation to give *p*-nitrosophenol. The latter gives rise to *p*-nitrophenol as the predominant final product.

For anisole, nitration in the mixture of nitric, sulfuric, and acetic acids at room temperature leads to 2-nitroanisole (25%) and 4-nitroanisole (65%), with some by-products of unidentified structures. In the presence of sodium azide as a scavenger for nitrous acid (which is usually contained in nitric acid), no reaction took place. So the process proceeds through a nitrous acid–catalyzed reaction (see later). During the nitration of anisole with ^{15}N-enriched nitric acid in sulfuric and acetic acids mixture, the ^{15}N NMR signals of 2- and 4-nitroanisole exhibit emission indicating their formation by recombination of anisole cation-radical with nitrogen dioxide radical. It is concluded from the magnitude of ^{15}N CIDNP effect that 2-nitroanisole is formed only via coupling of ion-radical with radical, whereas 3-nitroanisole can also be formed via a nonradical pathway through a direct attack of nitronium cation on neutral anisole. The probability of the latter pathway is estimated to an extent of 60% (Lehnig 1997).

Aromatic *N*,*N*-dialkylamines react rapidly with HNO_2 and undergo ring nitration and nitrosative dealkylation; both reactions are linked through the formation of a nitrosoammonium ion $R^1R^2_2N^+$–N=O (R^1=Ar, R^2=Alk). This nitrosoammonium ion then undergoes reversible homolysis to NO and a cation-radical (Loeppky et al. 1998).

Nitrous acid catalysis also takes place in the nitration of such compounds (naphthalene) that are unable to undergo nitrosation on the given conditions or whose nitrosation proceeds slower than nitration. As accepted, the nitrosonium ion is formed from HNO_2 in acid media. The nitrosonium ion oxidizes an aromatic substrate into a cation-radical and transforms into nitric oxide. The latter reduces nitronium cation to nitrogen dioxide that gives a σ-complex with the aromatic cation-radical:

$$HONO + H^+ \rightarrow H_2O + NO^+$$

$$ArH + NO^+ \rightarrow ArH^{+\bullet} + NO^\bullet$$

$$(NO^{\bullet} + NO_2^{+} \rightarrow NO^{+} + NO_2^{\bullet})$$

$$ArH^{+\bullet} + NO_2^{\bullet} \rightarrow Ar(H)NO_2^{+} \rightarrow H^{+} + ArNO_2$$

The reaction ($NO^{\bullet} + NO_2^{+} \rightarrow NO^{+} + NO_2^{\bullet}$) is recommended by Ridd (1998) to put in parentheses to imply that it illustrates the stoichiometry of the process, not the mechanism. The mechanism is more complex because the rate of these nitrous acid–catalyzed nitrations greatly exceed the rate of formation of nitronium ions in the solution.

The preceding sequence of mechanistic steps has been experimentally proved for nitration of a wide range of organic compounds (Ridd 1991, Ridd and Sandall 1981, Clemens et al. 1984, 1985b, Clemens et al. 1985a, Lehnig 1996, 1997, Giffney and Ridd 1979, Powell et al. 1990). Some examples deserve special consideration.

A kinetic study of nitrous acid–catalyzed nitration of naphthalene with an excess of nitric acid in aqueous mixture of sulfuric and acetic acids (Leis et al. 1988) shows a transition from first-order to second-order kinetics with respect to naphthalene. (At this acidity, the rate of reaction through the nitronium ion is too slow to be significant; the amount of nitrous acid is sufficient to make one-electron oxidation of naphthalene as the main reaction path.) The reaction that initially had the first-order in respect to naphthalene becomes the second-order reaction. The electron transfer from naphthalene to NO^{+} has an equilibrium (reversible) character. In excess of the substrate, the equilibrium shifts to the right. A cause of the shift is the stabilization of cation-radical by uncharged naphthalene. The stabilized cation-radical dimer $(NaphH)_2^{+\bullet}$ is just involved in nitration:

$$NaphH + NaphH + NO^{+} = (NaphH)_2^{+\bullet} + NO^{\bullet}$$

$$(NO^{\bullet} + NO_2^{+} \rightarrow NO^{+} + NO_2^{\bullet})$$

$$(NaphH)_2^{+\bullet} + NO_2^{\bullet} \rightarrow NaphNO_2 + NaphH + H^{+}$$

Therefore, one-electron oxidation of naphthalene by NO^{+} is the rate-determining stage at low naphthalene concentrations (= means equilibrium of this oxidation). At high naphthalene concentrations, the rate of the process no longer depends on the rate of accumulation of cation-radical species. In this case, the rate depends on recombination of the species with $^{\bullet}NO_2$ radical. The authors point out that "for many of the more reactive aromatic compounds, reaction paths involving electron transfer in nitration will become more important as the concentration of the aromatic compound is increased, irrespective of the concentration of the species accepting the electron" (Leis et al. 1988).

Nitration of mesitylene by means of $H^{15}NO_3$ in the mixture of CF_3COOH with 10% H_2O yields nitro mesitylene with no nuclear polarization (Clemens et al. 1985a). However, the same product with a very strong ^{15}N polarization is obtained after addition of nitrous acid. Nitrosonium cation oxidizes mesitylene, then ion-radical pair [$ArH^{+\bullet}$ $NO_2^{\bullet}$] is formed. There is evidence (Eberson and Radner 1980) that the reaction of naphthalene cation-radical with nitrogen dioxide is slower than a diffusion-controlled process. Hence, [$ArH^{+\bullet}$ $NO_2^{\bullet}$] is formed at the expense of components approaching one another, and the pair for definite time moves independently. Without such separation of ion-radical pair, no nuclear polarization effect can be observed. This underlines that when these pairs are already formed, they (or some part of them) do not pass immediately on to form the nitro compound (Ridd 1991). The mesitylene cation-radical, which exists as an intermediate in the reaction under consideration, gives by-products, too—methyl derivatives of nitro diphenylmethane and compounds bearing the nitro group in the side chain (Clemens et al. 1985a).

TABLE 4.4
Calculated Spin-Density Distribution (ρ_i) in Xylene Cation-Radicals and Determined Partial Factors (φ_i) of Ring-Attack Rates for Nitrations of Neutral Isomeric Xylenes with Nitric Acid in Acetic Anhydride

Xylene	$\rho_1(\varphi_1)$	$\rho_2(\varphi_2)$	$\rho_3(\varphi_3)$	$\rho_4(\varphi_4)$	$\rho_5(\varphi_5)$	$\rho_6(\varphi_6)$
1, 2	0.450	0.450	−0.310	0.360	0.358	−0.308
	(30)	(30)	(7)	(14)	(14)	(7)
1, 3	0.241	−0.152	0.241	0.539	−0.416	0.539
	(0.5)	(15)	(0.5)	(42)	(0)	(42)
1, 4	0.482	0.060	0.060	0.482	0.060	0.060
	(38)	(6)	(6)	(38)	(6)	(6)

Source: Calculated spin-density distribution (ρ_i)—Feng, J., Zheng, X., Zerner, M.C., *J. Org. Chem.*, 51, 4531, 1986; partial factors (φ_i)—Fisher, A. and Wright, G.J., *Austral. J. Chem.*, 27, 217, 1974).

4.5.4.2 System of HNO_3 and $(CH_3CO)_2O$

In this case, nitration takes place in solutions prepared by dissolving nitric acid in acetic anhydride. Acetyl nitrate is formed in these solutions:

$$HNO_3 + (CH_3CO)_2O \rightarrow CH_3COONO_2 + CH_3COOH$$

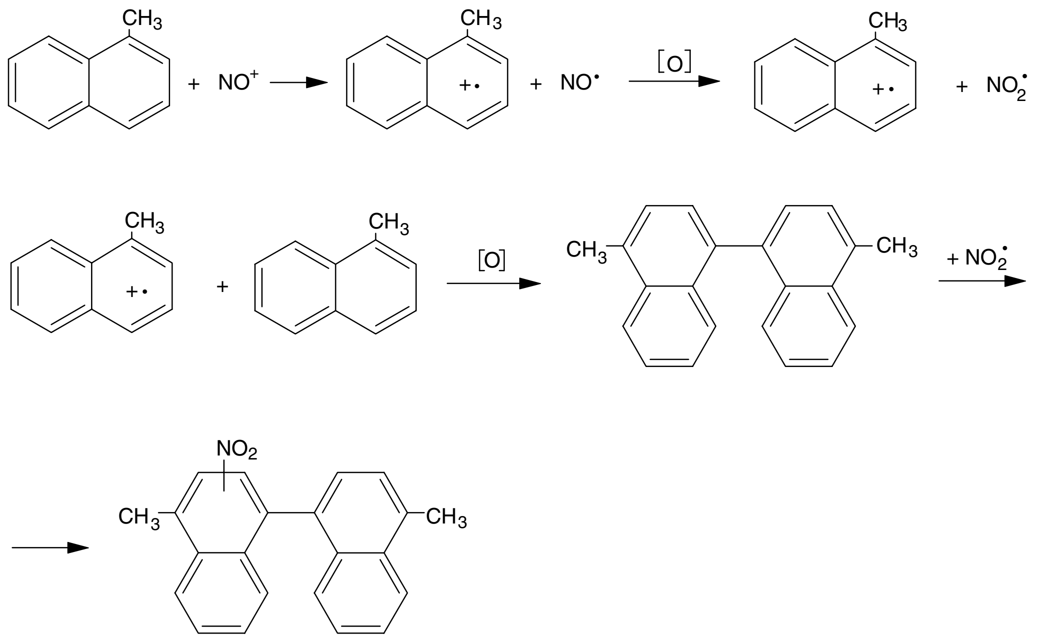
Such solutions are very potent nitrating mixtures and affect nitrations at higher rates than solutions of nitric acid in inert organic solvents. There are scarce data on the nature of nitrating species formed from acetylnitrate in the presence of aromatics. The existing data permit one to conclude that cation-radicals of xylenes play a role in nitration.

For nitration of aromatic hydrocarbons with acetylnitrate, there is a clear linear correlation between the IPs of these hydrocarbons and rate constants relative to benzene (Pedersen et al. 1973). Table 4.4 juxtaposes spin densities of cation-radicals and partial rate factors of ring attacks in the case of nitration of isomeric xylenes with nitric acid in acetic anhydride.

Table 4.4 helps us to understand why 1,4- and 1,2-xylenes undergo substitution in the ipso positions (the positions where the methyl groups are located). The electrophilic reagents obviously have to attack the substrate at the position with maximal electron density. These are ipso positions for the cation-radicals of 1,4- and 1,2-isomers. (For the neutral isomers, these are positions where the methyl groups are absent!) The substitution is directed into the ipso positions of 1,4-xylene and ring by up to 76 and 24% only, respectively. In case of 1,2-xylene, the substitution takes place for 60 and 40% at ipso-positions and into the ring, respectively. In 1,3-xylene cation-radical, spin density is maximal in the nonmethylated positions 4 and 6, which are involved in the substitution for 84% (Fisher and Wright 1974).

4.5.4.3 System of $NaNO_2$ and CF_3SO_3H

The title system in AN forms a homogeneous solution. The generation of NO^+ cation takes place. As known, NO^+ is a remarkable, diverse reagent not only for nitrosation and nitration but also for oxidation. Kochi et al. (1973) christened a new general mechanism "oxidative aromatic substitution" to describe aromatic substitution reactions (Kochi 1990, Bosch and Kochi 1994). This mechanism incorporates ground-state electron transfer before the substitution step (see also Skokov and Wheeler 1999).



SCHEME 4.42

Tanaka et al. (1996, 2000) studied the behavior of a series of naphthalene derivatives in AN solution containing $NaNO_2$ and CF_3SO_3H at 0°C in air. Naphthalene showed very low reactivity, and most of the starting material was recovered after the reaction. In case of 1-methylnaphthalene, a coupling reaction took place to produce 4,4′-dimethyl-1,1′-binaphthyl in 97% yield alongside mononitro derivatives of the dimer in 1.5% yield. However, when the reaction is carried out on the same conditions but in inert (N_2) atmosphere, the yield of the dimer decreased from 97 to 15%, and no mononitro derivatives were formed. Therefore, the oxidation of NO with O_2 to form NO_2 (after the electron transfer to NO^+ from 1-methylnaphthalene) is an obvious step of the reaction depicted in Scheme 4.42.

It is interesting to compare the results depicted in Scheme 4.42 with those of the reactions of the same substrate with $NOBF_4$ in the presence or absence of CF_3SO_3H. In the presence of CF_3SO_3H, 4,4′-dimethyl-1,1′-binaphthyl was obtained as the sole product with excellent yield (more than 90%). However, in the absence of CF_3SO_3H, only a small amount of 1-methylnaphthalene was converted to mononitro 4-methylnaphthalene (5%) and 4,4′-dimethyl-1,1′-binaphthyl (up to 1%). The unreacted substrate was recovered (Tanaka et al. 1996).

Hence, CF_3SO_3H plays two roles in the reactions considered. First, it produces NO^+ from $NaNO_2$. Second, it inhibits the nitration by trapping of NO_2 (or N_2O_4, i.e., $NO^+NO_3^-$):

$$NaNO_2 + 2CF_3SO_3H \rightarrow CF_3SO_3NO + CF_3SO_3Na + H_2O$$

$$CF_3SO_3NO \rightarrow CF_3SO_3^- + NO^+$$

$$NO^+ + e \rightarrow NO^\bullet$$

$$NO^\bullet + O_2 \rightarrow 2NO_2^\bullet$$

$$2NO_2^\bullet = N_2O_4 = NO^+NO_3^-$$

$$NO^+NO_3^- + 2CF_3SO_3H \rightarrow CF_3SO_3NO + CF_3SO_3NO_2 + H_2O$$

In terms of nitration, the system ($NaNO_2$ + CF_3SO_3H) is of no interest. At the same time, dimerization in this system can be attractive. For the last direction, CF_3SO_3H (or FSO_3H) is necessary to produce binaphthyl derivatives more preferentially than nitro compounds (Tanaka et al. 1996). This work was preceded by the observation that the reaction of $NO^+AlCl_4^-$ with 1-methyl-, 1,2-dimethyl-, 1,3-dimethyl, or 1,8-dimethylnaphthalenes in liquid SO_2 leads to a partial α,α-dimerization (see Borodkin et al. 1993). Ozeryanskii et al. (1998) published the dimerization of 1,8-*N*,*N*-bis(d imethylamino)naphthalene by the action of $^{\bullet}NO_2$ in $CHCl_3$. This reaction is accompanied by the formation of 4-nitro-1,8-*N*,*N*-bis(dimethylamino)naphthalene. Both groups of authors consider cation-radicals of the initial substrates as intermediate species.

Tanaka et al. (2000) reported that NO_2^+ nitration of 1,8-dimethylnaphthalene leads to 2-nitro and 4-nitro products. For 2-nitro product, the reaction proceeds as electrophilic substitution—the nitro group comes into the ipso position and then migrates to the position 2, thus giving the final product. For 4-nitro product, the process develops according to electron-transfer route. The spin density of 1,8-dimethylnaphthalene cation-radical is highest at position 4 (or, the same, at position 5). It is the para nitration that takes place in the experiment.

4.5.4.4 Systems of Metal Nitrites with Oxidizers

Aromatic cation-radicals can also react with NO_2^-, giving nitro compounds. Such reactions proceed either with a preliminary prepared cation-radical or starting from uncharged compound if iodine and silver nitrite are added. As for mechanisms, two of them seem feasible—first, single electron transfer from the nitrite ion to a cation-radical and second, nitration of ArH with the $NO_2^{\bullet}$ radical. This radical is quantitatively formed when iodine oxidizes silver nitrite in carbon tetrachloride (Neelmeyer 1904).

Cation-radicals of naphthalene and its homologues, pyrene, or perylene react with NO_2^- ion in AN, giving electron-transfer products, that is, ArH and $NO_2^{\bullet}$. The latter radical is not very active in these reactions and nitration takes place only with extremely reactive compounds such as perylene (Eberson and Radner 1985, 1986). This mechanism is seemingly distinctive of compounds with E° less or equal to 1 V in AN (or in other solvents solvating NO_2^- ions sparingly).

An attempt to combine electrochemical and micellar-catalytic methods is interesting from the point of view of the mechanism of anode nitration of 1,4-dimethoxybenzene with sodium nitrite (Laurent et al. 1984). The reaction was performed in a mixture of water in the presence of 2% surface-active compounds of cationic, anionic, or neutral nature. It was established that 1,4-dimethoxy-2-nitrobenzene (the product) was formed only in the region of potentials corresponding to simultaneous electrooxidation of the substrate to the cation-radical and the nitrite ion to the nitrogen dioxide radical (1.5 V versus saturated calomel electrode). At potentials of oxidation of the sole nitrite ion (0.8 V), no nitration was observed. Consequently, radical substitution in the neutral substrate does not take place. Two feasible mechanisms remain for addition to the cation-radical form, as follows:

$$ArH^{+\bullet} + NO_2^- \rightarrow [Ar(H)NO_2]^{\bullet} - e \rightarrow Ar(H)NO_2]^{+} \rightarrow H^{+} + ArNO_2$$

$$\uparrow$$

$$ArH^{+\bullet} + NO_2^{\bullet}$$

Micellar catalytic methods were used to operate a choice between these two mechanisms. When an ion-radical has a charge opposite to that of the micelle surface, it is trapped by the micelle (Okamoto et al. 2001). In the presence of a surface-active compound, the aromatic substrate is nitrated in the very depth of a micelle, and the reaction rate depends on the local concentration of the nitrating agent on phase boundaries between the micelle and solution. A positively charged

micelle will have a higher concentration of the nitrite anion. However, such a micelle is less likely to include the substrate cation-radical, which also bears a positive charge. A negatively charged micelle should assist in the insertion of the cation-radical and repel the nitrite ion. If nitration proceeds with the participation of the neutral radical $NO_2^{\bullet}$, the sign of the micelle charge cannot be significant (for instance, chemical treatment of 1,4-dimethoxybenzene with gaseous nitrogen dioxide, by bubbling through the micellar system, gives rise to the nitro product in the same yields irrespective of the micelle charge.)

For the anode process at comparable conditions, the yield of 1,2-dimethoxy-2-nitrobenzene depends distinctly on the electrical nature of a micelle. Namely, the yields are equal to 30, 40, and 70% for the positively, negatively, and neutrally charged micelles, respectively. The observed micellar effect corroborates the mechanism that includes 1,4-dimethoxybenzene cation-radical and nitrogen dioxide radical as reacting species.

4.5.4.5 Systems of Metal Nitrates with Oxidizers

As known (Addison and Logan 1964), anhydrous nitrates exhibit oxidizing properties. Their oxidizing activity increases from ionic nitrates with alkali and alkali-earth metal cations to covalent nitrates with transient metal cations. Oxidation reactions result in the formation of nitrogen-containing oxides. Depending on the kind of a nitrate salt and reaction conditions, one of these oxides can be predominant. Organic substrates can evidently serve as reductant.

A promising practical variant of such a process is aromatic nitration by the use of solid supports. Microporous solids such as silica, alumina, and alumosilicates offer a wide range of active sites for catalysis, and most of them can be regenerated if deactivated during a reaction. Delaude et al. (1993) underline that a substrate of the reaction migrates to catalytic sites. This reduces the activation energy. The geometric consequence of anchoring onto a solid is to restrict the angles of attack, that is, to enhance selectivity. Nitration of phenols gives an example of the enhanced selectivity.

Conventional nitration of phenol results in the formation of ca. 67% *ortho*- and 33% *para*-nitrophenols. This corresponds to statistical distribution in substitution. (It is worth noting that only one of these isomers, namely *p*-nitrophenol is the desired product.) Thus, the challenge is to reverse the distribution into predominantly para preference. The ion-radical route of nitration approaches this. As Dewar et al. (1985) have shown, the phenol cation-radical differs from the uncharged phenol molecule with enhanced reactivity of the para position. In the cation-radical, the spin density appears to be greater in the para position than in the ortho one. To guide the system along this route, Cornelis and Laszlo (1985) devised a rather efficient heterogeneous nitration procedure. The main ingredient is clayfen, that is, montmorillonite clay (K10) supported ferric nitrate. The authors point out that the clay, the ferric ions with which it is doped, and nitrosonium ions that it evolves are all oxidants cooperating to preoxidize the substrate into the corresponding cation-radical. Indeed, the phenol clayfen nitration led to significant improvements in yields and desired selectivity with respect to common procedures.

To elevate *p*-selectivity in nitration of toluene is another important task. Commercial production of *p*-nitrotoluene up to now leads with twofold amount to the unwanted *o*-isomer. This stems from the statistical percentage of *o*:*m*:*p* nitration (63:3:34). Delaude et al. (1993) enumerate such a relative distribution of the unpaired electron densities in the toluene cation-radical—ipso 1/3, ortho 1/12, meta 1/12, and para 1/3. As seen, the para position is the one favored for nitration by the attack of $NO^{\bullet}$ (or $NO_2^{\bullet}$) radical. A procedure was described (Delaude et al. 1993) that used montmorillonite clay supported copper (cupric) nitrate (claycop) in the presence of acetic anhydride (to remove excess humidity) and with carbon tetrachloride as a medium, at room temperature. Nitrotoluene was isolated almost quantitatively with 23:1:76 ratio of ortho/meta/para mononitrotoluene.

Using acyl nitrates as nitrating agents (compare with Section 4.5.4.2) and zeolite H-ZSM-11 treated with tributylamine, Nagy et al. (1991, 1994) were able to nitrate toluene with an even more impressive percentage of the isomers obtained—ortho 2–3%, meta 1–2%, and para 95–98%.

Samajdar et al. (2000) performed nitration of aromatic compounds by bismuth nitrate on catalysis with montmorillonite KSF. The reaction develops in THF suspension on steering during 10 min. Nitration of anisole proceeds strictly in the para position (91% yield after 10 min), but in case of phenol, the reaction occurs to be nonregioselective and 3:1 mixture of para and ortho nitro products is formed with a common yield of 89%. Nitration of estrone (the steroid phenol) also leads to 1:1 mixture of para and ortho nitrophenolic steroids in 94% yield.

Bismuth nitrate itself can act as a nitrating agent for phenols in solid-state reactions initiated by grinding. Thus, *p*-methyl and *p*-chlorophenol are nitrated in the ortho positions with respect to hydroxyl group on grinding at room temperature during less than 5 min. The isolated yields were 63 and 88%, respectively (Sun et al. 2005). Formation of ion-radicals on grinding has been considered on pages 92–96 of another monograph by me specially devoted to organic reactions initiated by mechanical action (Todres 2006). It deserves only to note here that the solid-state reactions are more ecological friendly than the reactions in solutions. They avoid hazardous problems and the necessity to dispose the large amount of acidic wastes.

4.5.4.6 Systems with Tetranitromethane as Nitrating Agent

Nitration with tetranitromethane proceeds along the ion-radical route. Tetranitromethane is a smooth nitrating agent and mild oxidizer. It is convenient for nitration of highly activated substrates such as phenols, azulene, and heterocycles in the presence of pyridine, *N*,*N*-dialkylaniline, etc. As shown (Morkovnik 1988), these reactions include one-electron transfer:

$$ArH + C(NO_2)_4 \rightarrow [ArH \cdots C(NO_2)_4] \rightarrow [ArH^{+\bullet}, C(NO_2)_4^{-\bullet}] \rightarrow [ArH^{+\bullet}, NO_2^{\bullet}, C(NO_2)_3^{-}]$$

The photochemical addition of tetranitromethane to aromatic compounds under conditions of excitation of the $[ArH \cdots C(NO_2)_4]$ charge-transfer complex by light matching the wavelength of the charge-transfer band results in a recombination within $[ArH^{+\bullet}, NO_2^{\bullet}, C(NO_2)_3^{-}]$ triad. The destiny of triad depends on the nature of the solvent (Sankararaman et al. 1987, Sankararaman and Kochi 1991). In dissociating solvents, radical substitution is predominant, leading to nitro products and trinitromethane:

$$[ArH^{+\bullet}, NO_2^{\bullet}, C(NO_2)_3^{-}] \rightarrow ArNO_2 + HC(NO_2)_3$$

In nondissociating solvents, the main process consists of ion-pair reaction that results in the disengagement of nitrous acid and formation of trinitromethylated products:

$$[ArH^{+\bullet}, NO_2^{\bullet}, C(NO_2)_3^{-}] \rightarrow HNO_2 + ArC(NO_2)_3$$

The addition of a low amount of trifluoroacetic acid results in fast protonation of $C(NO_2)_3^{-}$. The major follow-up reaction now becomes the slower reaction between $ArH^{+\bullet}$ and $NO_2^{\bullet}$ (Eberson et al. 1996).

The activity of $NO_2^{\bullet}$ radical is quite moderate. The leading role belongs to anion $C(NO_2)_3^{-}$. On disintegration of the ternary complex, this anion departs with proton (the light particle). During the reaction within the triad, $ArH^{+\bullet}$ couples predominantly with $C(NO_2)_3^{-}$ rather than with $NO_2^{\bullet}$. Addition of tetrabutyl ammonium perchlorate results in the binding of $C(NO_2)_3^{-}$ anion with Bu_4N^{+} cation. This binding entirely suppresses alkylation, and nitration remains the sole direction.

Studies of interactions between tetranitromethane and aryl derivatives of magnesium, tin, and mercury in sulfolane (Shevelyov et al. 1974, 1975) confirm that $NO_2^{\bullet}$ radical has some slight activity. For example, the reaction of diarylmercury with tetranitromethane passes through a transient step with the formation of radicals $Ar^{\bullet}$ and $NO_2^{\bullet}$. These radicals almost do not interact:

$$Ar{-}Hg{-}Ar + C(NO_2)_4 \rightarrow [Ar^{\bullet}, ArHg^{+}, NO_2^{\bullet}, C(NO_2)_3^{-}] \rightarrow Ar^{\bullet} + ArHgC(NO_2)_3 + NO_2^{\bullet}$$

The major route of $Ar^{\bullet}$ transformation is $H^{\bullet}$ abstraction from the solvent with formation of ArH.

4.5.4.7 Systems with Participation of Nitrogen Dioxide

The paramagnetic dioxide $^{\bullet}NO_2$ is in equilibrium with diamagnetic dimer N_2O_4. At normal pressure, the percentage of $^{\bullet}NO_2$ in the equilibrium mixture is 31 at 40°C, 88 at 100°C, and 100 above 140°C. The liquid mixture contains mainly N_2O_4, and the solid is the dimer entirely. Because of the equilibrium, reaction paths through N_2O_4 lead to the same products as the reaction through $^{\bullet}NO_2$ (see, e.g., Chatterjee et al 1995).

In 1,1,1,3,3,3-hexafluoropropan-2-ol, the reaction of 1,4-dimethoxy-2,3-dimethylbenzene with a deficit of nitrogen dioxide gives a high concentration of the aromatic cation-radical, which lives long enough and can be detected spectroscopically. In the presence of excessive amounts of $^{\bullet}NO_2$, this cation-radical decays rapidly giving the 5-nitro derivative of the starting compound (Eberson et al. 1996).

Kinetic characteristics are obtained for the reaction between several polycyclic aromatic hydrocarbons with nitrogen dioxide in dichloromethane at 25°C. They are in accord with the intermediate formation of the cation-radicals (Pryor et al 1984).

Considering nitration with the help of NO_2/N_2O_4 in an aprotic medium, one should avoid a simplified approach to its mechanism. The dissociation equilibrium $N_2O_4 = 2NO_2^{\bullet}$ is characterized at 298.15 K (25°C) with constants, on molality basis, 3.5×10^{-5} in hexane, 5.9×10^{-6} in carbon tetrachloride, and 5.3×10^{-6} in chloroform (Mendiara and Perissinotti 2003). In aprotic mediums, two ionic routes of dissociation of N_2O_4 are possible

$$NO^+ + NO_3^- \leftarrow N_2O_4 \rightarrow NO_2^+ + NO_2^-$$

In the presence of water (even in traces), acids are generated

$$N_2O_4 + H_2O \rightarrow HNO_3 + HNO_2$$

The acidity constants of HNO_3 and HNO_2 are the following: $pK^{H^+}(HNO_3) = 16.0$ and $pK^{H^+}(HNO_2) = 20.6$ at 30°C in sulfolane (Boughriet et al. 1987). The authors deduced the equilibrium constants (K) for N_2O_4 and N_2O_3 reactions:

$$N_2O_4 + H^+ = HNO_3 + NO^+ \; (K = 6.3 \times 10^8)$$

$$N_2O_4 + H^+ = HNO_2 + NO_2^+ \; (K = 4.0 \times 10^{-2})$$

$$N_2O_4 + HNO_2 = HNO_3 + N_2O_3 \; (K = 2.5 \times 10^{-1})$$

$$N_2O_3 + H^+ = HNO_2 + NO^+ \; (K = 2.5 \times 10^9)$$

Hence, all of the reactions are probable and takes place in corresponding proportion.

Dinitrogen trioxide undergoes both radical and ion dissociation in aprotic solvents (e.g., in sulfolane):

$$N_2O_3 \rightarrow NO^{\bullet} + NO_2^{\bullet}$$

$$N_2O_3 \rightarrow NO^+ + NO_2^-$$

Nitration of naphthalene (NaphH) by means of dinitrogen tetroxide is described as follows:

$$NaphH + 2N_2O_4 \rightarrow NaphNO_2 + HNO_3 + N_2O_3$$

This reaction is irreversible, but it is attended with an equilibrium:

$$N_2O_3 + HNO_3 = HNO_2 + N_2O_4$$

Consequently, this nitration obeys the following equation:

$$\text{NaphH} + N_2O_4 \rightarrow \text{NaphNO}_2 + HNO_2$$

In reality, nitration of naphthalene with dinitrogen tetroxide in an aprotic medium is a complex process. The leading role belongs to nitrosyl cation. This species is a strong oxidant acting according to the outer-sphere mechanism (compare with Section 1.7.10):

$$\text{NaphH} + {}^{+}\text{N=O} \rightarrow \text{NaphH} \cdots {}^{+}\text{N=O} \rightarrow \text{NaphH}^{+\bullet} + {}^{\bullet}\text{N–O, etc.}$$

4.5.4.8 Nitration and Hydroxylation by Peroxynitrite

Peroxynitrite ($ONOO^-$) is a cytoxic species that is considered to form nitric oxide (NO) and superoxide ($O_2^{-\bullet}$) in biological systems (Beckman et al. 1990). The toxicity of this compound is attributed to its ability to oxidize, nitrate, and hydroxylate biomolecules. Tyrosine is nitrated to form 3-nitrotyrosine (Ramazanian et al. 1996). Phenylalanine is hydroxylated to yield *o*-, *m*-, and *p*-tyrosines. Cysteine is oxidized to give cystine (Radi et al. 1991a). Glutathione is converted to *S*-nitro- or *S*-nitroso derivatives (Balazy et al. 1998). Catecholamines are oxidatively polymerized to melanin (Daveu et al. 1997). Lipids are also oxidized (Radi 1991b) and DNA can be scissored by peroxynitrite (Szabo and Ohshima 1997).

Despite a considerable literature on the various modes of reactions induced by peroxynitrite, the kinetic and mechanistic aspects of these transformations have been clarified only recently (Nonoyama et al. 1999). The authors give the following picture of the peroxynitrite chemical behavior. In alkaline solutions, peroxynitrite is a stable anionic species. At physiological pH, it is rapidly protonated to form peroxynitrous acid (ONOOH): $ONOO^- + H^+ \rightarrow ONOOH$.

This acid undergoes homolytic decomposition to $^{\bullet}OH$ and $^{\bullet}NO_2$ radical species:

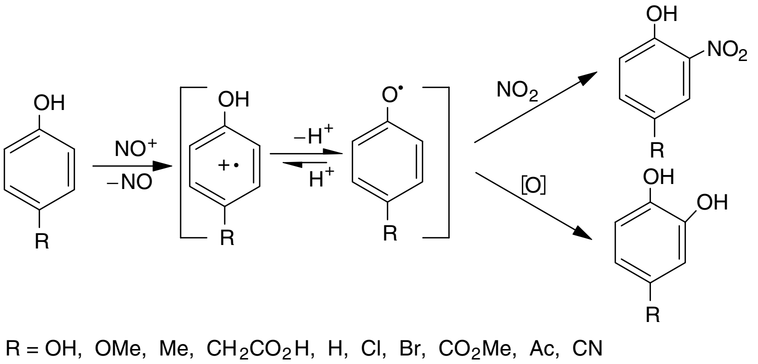
$$ONOOH \rightarrow {}^{\bullet}OH + {}^{\bullet}NO_2$$

Heterolytic decomposition of the acid is also possible; Pryor and Squadrito (1995) connect this direction with the generation of a high-energy intermediate $[ONOOH]^*$: $NO_2^+ + {}^-OH \rightarrow [ONOOH]^* \rightarrow NO^+ + {}^-OOH$. Interactions between such generated species eventually lead to the formation of NO^+ and NO_3^- ions:

$$ONOO^- + NO^+ \rightarrow 2NO_2$$

$$2NO_2 \rightarrow N_2O_4 \rightarrow NO^+ + NO_3^-$$

To gain insight into how peroxynitrite attacks activated aromatic substrates, Nonoyama et al. (1999) examined the kinetic features of the reaction of peroxynitrite with para-substituted phenols. The authors used ONOONa as a reagent. The latter was prepared by ozonolysis of sodium azide in aqueous solution at pH 12. The reactions with substituted phenols were performed in aqueous phosphate buffer or in AN, and the nature and yields of the resulting products were determined. The major products were the corresponding 2-nitro and 2-hydroxy derivatives of the starting phenols. Kinetic study showed a good correlation with Hammett σ_p^+ parameters and reduction potentials of the substrates. The cation-radical mechanism was proposed involving the following key species: the nitrosonium



SCHEME 4.43

ion (NO^+) as the initial elecrophile generated from the peroxynitrous anion, cation-radicals formed as a result of the oxidative action of NO^+ on the phenolic substrates, and $^{\bullet}NO_2$ radical as a nitrating agent to these cation-radicals (Scheme 4.43).

4.5.4.9 Gas-Phase Nitration

Gas-phase nitration is important from theoretical and practical points of view. In solution, the solvation of the small nitronium ion should exceed that of the large aromatic cation-radical, and hence electron transfer should be less probable. In the gas-phase process, the solvation is absent and only inner reorganization energy remains significant.

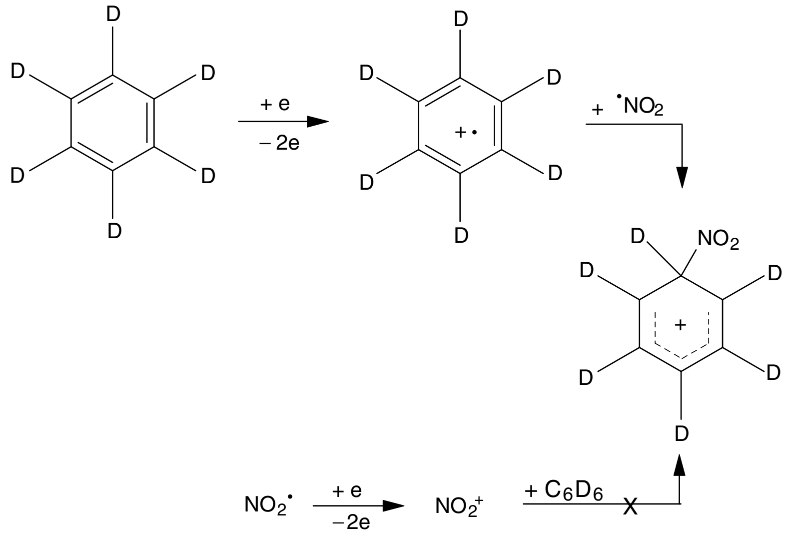
Gas-phase nitration of aromatic compounds by nitrogen dioxide or with the nitrating mixture is a serious ecological problem. It proceeds simultaneously in the atmosphere and results in the formation of cancer-producing components in air (Warnek 1988). Aromatic compounds are the products of incomplete combustion of fuels. Aromatics are the usual pollutants of chemical, petroleum, and coal-pyrogenic industries. These compounds are permanently present in air. As for NO_2 in air, its presence is always sufficient. Air sols of HCl and H_2SO_4 are also present. In addition to sulfuric acid, nitric acid (the second component of the nitrating mixture) is formed as a result of the following reaction:

$$NO_2 + 2O_3 + HCl \rightarrow ClO + 2O_2 + HNO_3$$

Adsorption of nitric and sulfuric acids on ice particles provides the sol of the nitrating mixture. An important catalyst of aromatic nitration, nitrous acid, is typical for polluted atmospheres. Combustion sources contribute to air pollution via soot and NO_x emissions. The observed formation of HNO_2 results from the reduction of nitrogen oxides in the presence of water by C—O and C—H groups in soot (Ammann et al. 1998). As seen, gas-phase nitration is important ecologically.

De Queiroz et al. (2006) performed mass-spectrometric experiments in which gas-phase reactions of the isolated NO_2^+ and benzene derivatives were studied. The reaction results in the predominant electron abstraction yielding exclusively ionized benzenes. None of the expected adducts (such as σ complexes) were observed. Probably because direct addition of NO_2^+ to benzene is strongly exothermic, the nascent product is too hot to survive when it is isolated in the gas phase.

Benezra et al. (1970) did observe $(C_6D_6NO_2)^+$ σ-complex formed in the gaseous mixture of nitrogen dioxide with perdeuterobenzene. The complex origin was studied by the method of ion-cyclotron resonance. The rate of the σ-complex formation depends only on the rate of formation of perdeuterobenzene cation-radicals but not nitronium ions. Hence, σ-complex has its origin from the pair of $NO_2^{\bullet} + (C_6D_6)^{+\bullet}$ and not from the pair of $NO_2^+ + C_6D_6$. If ionization is performed in vapor compositions containing pyridine or THF, protonation of these additives occurs. Decrease of $(C_6D_6NO_2)^+$ ion, but not $(C_6D_6)^{+\bullet}$ ion-radical, takes place. Studies of benzene homologues produce



SCHEME 4.44

analogous results (Schmitt et al. 1984). This confirms the structure of $(C_6D_6NO_2)^+$ complex with an easily ionizing deuteron at the tetrahedral carbon atom (Scheme 4.44).

According to the works by Ausloos and Lias (1978) and De Queiros et al. (2006), the main process of $NO_2^+ + C_6H_6$ interaction leads to $NO_2^\bullet + (C_6H_6)^{+\bullet}$ for 70%. The collateral reaction affects 30% and produces $NO^\bullet + C_6H_5(H)O^+$. Obviously, intermediates, which are formed in the gaseous phase, arise as a result of the strong electrostatic attraction of species with no solvation. Calculations predict that incoming of the nitronium ion to benzene causes an interaction of frontal MOs. As a result, their energetic levels are changed. At a distance between the reagents from 0.025 to 0.015 nm, an electron transfer is possible, even from benzene to the nitronium ion (D'yachenko and Ioffe 1976). Such a transfer is energetically allowed. The energy of the lowest unoccupied orbital of the nitronium ion (−11 eV) is below that of the highest occuppied orbital of benzene (−9.24 eV). In principle, one π-electron can be moved from benzene to nitronium ion (Nagakura and Tanaka 1954). This point of view was developed in the later publications (Nagakura and Tanaka 1959, Nagakura 1963) and by other authors (Brown 1959, Takabe et al. 1976). As a result, the nitronium cation gives a radical species, that is, nitrogen dioxide, and benzene transforms into its cation-radical. This redox process takes place in the gaseous phase. Conjunction of both the particles, which are radicals in their nature, leads to σ-complex and then to substitution product.

Having in mind the mentioned importance of gas-phase aromatic nitration, it should be useful to arrange benzene derivatives as electron donor with respect to nitronium ion, using IPs. These potentials have been measured in the gaseous phase and can be extracted from NIST Chemistry WebBook (Lindstrom and Mallard, 2003). The data provide an indication for the thermodynamic feasibility of their one-electron oxidation by nitronium cation.

Namely, such a reaction is thermodynamically favored for benzene (IP = −32.98 kJ · mol^{-1}), toluene (IP = −73.07 kJ · mol^{-1}), phenol (IP = −107.72 kJ · mol^{-1}), anisole (IP = −133.59 kJ · mol^{-1}), and aniline (IP = −179.86 kJ · mol^{-1}). The unfavorable data are the following: nitrobenzene (IP = +34.11 kJ · mol^{-1}), benzonitrile (IP = +13.88 kJ · mol^{-1}), and benzotrifluoride (IP = +9.53 kJ · mol^{-1}).

Further, if the rate-determining step involves single-electron transfer, isotope effects should not affect the nitration rate, that is, k_H/k_D should be 1. Using ion-cyclotron resonance for studying aromatic nitration in the gas phase, Dunbar et al. (1972) found no isotope effect.

Let us give a concise inference. Although aromatic nitration is a typical reaction for a wide number of substrates, it cannot be considered a process with a single mechanism in all cases.

The ion-radical mechanism is characteristic in cases of substrates, which are ready for one-electron oxidation and capable to give stable cation-radicals in appropriate solvents. As the cited examples show, such a mechanism can really be revealed. However, very rapid transformations of aromatic cation-radicals can mask the ion-radical nature of many other reactions and create an illusion of their nonradical character. At the same time, the ion-radical mechanism demands its own approaches for further optimization of commercially important cases of nitration. This mechanism deserves our continued attention.

4.5.5 Meerwein and Sandmeyer Reactions

Reduction of arenediazonium salts provides the basis for a substantial number of chemical reactions. A notable application is the Sandmeyer reaction, which utilizes the diazo moiety to facilitate functionalization of aromatic systems and remains one of the most reliable transformations in organic chemistry. The general reaction involves the addition of the cuprate salt of the desired moiety to the diazonium species—$ArN_2^+ + CuX \rightarrow ArX$.

A large body of literature exists investigating the mechanism of the Sandmayer reaction, and as early as 1942, ion-radical mechanisms were thought to be applicable (Waters 1942). Kochi (1957) furthered this mechanistic interpretation, and the current consensus keeps this opinion (Galli 1988b, Weaver et al. 2001).

Meerwein reaction consists of condensation of ethylenic compounds with aryldiazonium salts in the presence of cupric and cuprous salts:

$$ArN_2Cl + {>}C{=}C{<} \rightarrow {>}C(Ar)C(Cl){<}$$

Ganushchak et al. (1972, 1984) proposed to perform the Meerwein chloroarylation of ethylenic compounds using the preliminarily prepared aryldiazonium tetrachlorocuprates. They found that methyl, ethyl, butyl acrylate, methyl methacrylate, and acrylonitrile in the polar solvent reacted with tetrachlorocuprate. Chloroarylation products were obtained with better yields than when using the traditional Meerwein reaction conditions.

The interaction of aryldiazonium tetrachlorocuprates [Cu(II)] with olefins has been studied by ESR spectroscopy using spin-trapping technique (Lyakhovich et al. 1991). The radicals $ArCH_2CH(^\bullet)Ph$ and $ArCH_2CH(^\bullet)CN$ have been detected in the mixtures of aryldiazonium tetrachlorocuprates [Cu(II)] with styrene and acrylonitrile using nitrosodurene as a spin adduct. However, aryl radical signals were not detected under these conditions. Obviously, aryl radicals react with the nearby ethylene bond within the activated ternary complex without leaving the solvent cage (Ganushchak et el. 1972, 1984). Note that Cu(II) salts in the modification of Meerwein reaction considered are not reduced to Cu(I) salts by solvents used in the reaction. At the same time, reduction of $CuCl_2$ by acetone plays an important role in the mechanistic description of Meerwein arylation because the resulting Cu(I) generates aromatic radicals (Kochi 1955):

$$CuCl_2 + CH_3COCH_3 \rightarrow CH_3COCH_2Cl + CuCl$$

$$ArN_2^+ + Cu(I) \rightarrow Ar^\bullet + Cu(II) + N_2$$

There are reasons to explain the catalytic activity of copper(II) in terms of cation-radical mechanism. This mechanism is confirmed by the unusual direction of Meerwein reaction in some cases, for example, when the replacement of halogen by an aryl radical occurs in the reaction of halostyrenes with aryldiazonium salts (Obushak et al. 1991). A cation-radical in the system [olefin-Cu(II)] has been detected by UV spectroscopy (Obushak et al. 1991). In the cases of cis isomers of benzylidenacetone (Allard and Levisalles 1972) and maleic esters (Isaev et al. 1972), the unreacted

part of the olefin comes back in the corresponding trans-form. This cis→trans isomerization is understandable if the olefin goes through the cation-radical state during the Meerwein reaction (Todres 1974).

Using the language of chemical symbols, the following schematic equations bring together the results on the mechanistic studies (Obushak et al. 1998, 2002):

$$\mathrm{ArN_2Cl + Cu(I) \rightarrow Ar^{\bullet} + N_2 + Cu(II) + Cl^-}$$

$$\mathrm{Cu(II) + {>}C{=}C{<} \rightarrow Cu(I) + [{>}C{=}C{<}]^{+\bullet}}$$

$$\mathrm{[{>}C{=}C{<}]^{+\bullet} + Ar^{\bullet} \rightarrow {>}C(Ar)\text{-}C^{\bullet}{<}}$$

$$\mathrm{Cl^- + Cu(II) \rightarrow Cl^{\bullet} + Cu(I)}$$

$$\mathrm{{>}C(Ar)\text{-}C^{\bullet}{<} + Cl^{\bullet} \rightarrow {>}C(Ar)\text{-}(Cl)C{<}}$$

In summary, the copper ion transfers an electron from the unsaturated substrate to the diazonium cation, and the newly formed diazonium radical quickly loses nitrogen. The aryl radical formed attacks the ethylenic bond within the active complexes that originated from aryldiazonium tetrachlorocuprate(II)-olefin or initial arydiazonium salt-catalyst-olefin associates and yields $\mathrm{{>}C(Ar)\text{-}C^{\bullet}{<}}$ radical. The latter was detected by the spin-trap ESR spectroscopy. The formation of both the cation-radical $\mathrm{[{>}C{=}C{<}]^{+\bullet}}$ and radical $\mathrm{{>}C(Ar)\text{-}C^{\bullet}{<}}$ as intermediates indicates that the reaction involves two catalytic cycles. In the other case, radical $\mathrm{{>}C(Ar)\text{-}C^{\bullet}{<}}$ will not be formed, being consumed in the following reaction:

$$\mathrm{Ar^{\bullet} + [{>}C{=}C{<}]^{+\bullet} \rightarrow {>}C(Ar)\text{-}C^{+}{<}}$$

The radical $\mathrm{{>}C(Ar)\text{-}C^{\bullet}{<}}$ is oxidized by ligand transfer as Jenkins and Kochi (1972) indicated. If the cation-radical $\mathrm{[{>}C{=}C{<}]^{+\bullet}}$ obtained as a result of the initial electron transfer is not fully consumed in the reaction, it is reduced by Cu(I) and returns in the form of its geometrical isomer. In the olefin cation-radical state, cis→trans conversion has to take place, and it indeed takes place in the systems considered (Obushak et al. 2002).

Analogous consideration of aryldiazonium salts and sulfur dioxide reaction with α-nitro olefins in the presence of cupric chloride gave rise to a conclusion that the process also includes the electron-transfer step and develops according to anion-radical mechanism (Bilaya et al. 2004). The reaction eventually leads to the formation of β-arylsulfonyl α-nitroethanes.

4.6 CONCLUSION

Our analysis of different ways to identify ion-radical reactions leads to the following conclusions:

1. None of the approaches can, by themselves and taken alone, identify an ion-radical conversion.
2. A set of suitable methods does give reliable information on the role that ion-radical stage plays in the net mechanism of a reaction.
3. A choice between the conventional (or classical) and ion-radical mechanism is a very important issue. The ion-radical pathway leads to products of the desired structure, makes the conversion conditions milder, or changes the reactivity of the secondary intermediate particles. If ion-radicals form and react in a solvent cage, reaction proceeds rapidly, product

yields are indistinguishable from standard schemes, then the role that ion-radicals play is only of theoretical interest, and thus it is not far essential for practical organic synthesis.

4. The ion-radical mechanism should be checked with respect to every individual reaction. Compounds of even one class may behave differently—some of them react by ion-radical mechanism, whereas others may take quite another pathway. At this point, it is very important to guess why the reaction chooses one or the other mechanism.
5. The results obtained by different methods for revealing a mechanism should agree. Only such an approach might uncover the mechanism chosen by a reaction.

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5 Regulating Ion-Radical Organic Reactions

5.1 INTRODUCTION

Ion-radical reactions require special methods to stimulate or impede them. The specificity of these methods is determined with particular properties of ion-radicals. Many ion-radical syntheses are highly selective yielding products unattainable by other methods. The aim of this chapter is to analyze the phenomena that determine the ways to optimize ion-radical reactions. This chapter considers factors governing the development of the reactions with proven ion-radical mechanisms. Two groups of optimizing factors will be discussed: physical and purely chemical ones. Factors such as solvent change and salt addition are certainly in the borderline between chemical and physical effects.

5.2 PHYSICAL EFFECTS

5.2.1 Effect of Light

There is clear evidence that electron excitation of reacting molecules accelerates the processes involving electron transfer (Endicott and Ramasami 1982, Juillard and Chanon 1983). A molecule becomes excited on absorbing a quantum of light. Electronically excited states of organic molecules are richer in energy than the corresponding ground states by 2–4 eV. Thus, photochemical reactions begin at an energy level much higher than that of thermal reactions. On photoirradiation, an electron in a donor occupies a higher orbital. The energy of the "external" electron increases, and so do the donating properties of the molecule. In other words, electron transfer to an acceptor becomes more probable. Of course, the acceptor molecule demonstrates the same change in electron configuration as a result of photoirradiation.

Reactions may be photoinitiated if the difference between the IP of a donor and electron affinity of an acceptor increases significantly. When the irradiation wavelength is chosen correctly, only donors out of touch with acceptors may be excited. In this case, the difference increases. This is often achieved by using irradiation in the spectral region corresponding to a charge-transfer band of a complex produced by a donor and an acceptor (Fox et al. 1983). Sometimes, substances that never react with each other become capable of forming charge-transfer complexes (CTCs) on electron excitation and then, to yield ion-radicals. However, we must also take into account that photoexcitation also involves significant electron redistribution, frequently. In photochemical processes, the ion-radical reactivity can be different from that in "normal" (chemical or electrochemical) reactions. Back electron transfer (see later) also plays a specifically important role in photoinduced reactions. This reversible process is not energetically favored under chemical generation of ion-radicals. Therefore, chemical or photochemical routes to ion-radicals often lead to absolutely different final products. The work by Ikeda et al. (2001) exemplified such a divergent reactivity.

Excited molecular complexes of the donor–acceptor type are called *excimers* if formed from identical molecules and *exiplexes* if originated from different molecules. From the theory, it is concluded that photochemical influence will more readily accelerate electron transfer in a weak donor–acceptor pair than in a strong pair (Juillard and Chanon 1983). An organic molecule in an electron-excited state is a more active oxidant or stronger reducer than the same molecule in a ground state.

Photoelectron transfer is usually described by the so-called Foerster's cycle: On transformation of a molecule into the excited state, the donor's IP is reduced by the value of the donor's excitation energy, and the acceptor's electron affinity increases by the value of the acceptor's excitation energy.

Compounds of enhanced excitability are used as sensitizers. When introduced into a reaction system of a donor and an acceptor, the sensitizer absorbs light. The sensitizer itself does not undergo bond breaking or isomerization and acts only as an oxidant or a reducer with regard to the substrate. For instance, 1-methoxynaphthalene is active as a reducer, whereas 1-cyanonaphthalene plays the role as an oxidant. A sensitizer's reducing ability increases when its valence electron is transferred from a relatively low-energy level to a rather high-energy level, which corresponds to the LUMO. The enforced oxidizing activity is also conditioned by a one-electron shift to the higher level, with the synchronous formation of a hole at the orbital left. For 1-cyanonaphthalene and related molecules, however, this energy increase is less significant than the growth of the electron affinity of the rising electron hole. In these sensitizers, the "abandoned" orbital is located low enough to make an electron transfer energetically favorable.

In general, a sensitizer transforms into its excited state, passes an excited electron (or hole) to a substrate, and then remains in the reaction sphere in the form of its ion-radical. Because both the ion-radicals formed bear opposite electric charges, they experience electrostatic attraction. Therefore, back electron transfer is a characteristic part of the whole process. Some authors even assume the bond formation at the expense of unpaired electrons of ion-radicals generated as a result of photoelectron transfer. This kind of bond formation just leads to a "bonded exiplex" (Wang et al. 2007). Particular emphasis should be placed on organic ions as sensitizers: They form radicals, not ion-radicals, as a result of the photoinduced electron transfer and the electrostatic interaction becomes impossible. (Possibility of the bonded-exciplex formation remains as a question.) Besides, simultaneous generations of cation- and anion-radical can direct the reaction to the exclusively radical route: A cation-radical is a strong proton donor and an anion-radical is a strong proton acceptor (see Section 1.3).

Of course, there are photoinduced electron-transfer reactions that proceed with no sensitizers. Thus, nitro aromatic anion-radicals can be generated by photoirradiation of the sodium dithionite mixture with a parent nitro compound in a strong alkaline solution (pH close to 13). Importantly, this method gives a strong ESR signal of the resulting anion-radical. The spectra have extremely narrow lines, with widths typically less than 0.01 mT. This is largely because oxygen (which can cause line broadening) is scavenged by excess dithionite (Corrie et al. 2000).

Rossi and de Rossi (1983) and Rossi et al. (1999) cited a substantial body of photoinduced ion-radical reactions of aromatic substitution. It is interesting herein to compare photoinduction and electrochemical stimulation of ion-radical reactions. As pointed out in Chapter 2, a mediator is used to take an electron from the cathode and transfer it onto a substrate. It is reasonable to do so if the substrate itself is not reduced at the cathode at the given potential. The same concern holds with anodic reactions that a mediator participates in. As seen, photosensitizing and electrocatalysis are quite close, differing in their electron origins or electron suckers. Electrochemical reduction or oxidation takes place at the electrode that can be described as a concentrated, long-living surface with an excess of electrons or electron holes. The photochemical excited state can be considered as containing a local "microelectrode" in an organic molecule. In comparison with a macroelectrode (cathode, anode), this "microelectrode" has a shorter lifetime and an essentially lower concentration. Despite that, the "microelectrode" appears to be very effective because it is distributed between all solvent cages and is occasionally connected directly with a substrate in a charge-transfer complex (CTC).

Hence, the influence of light initiates a one-electron transfer between a reactant and substrate. This results in the formation of a substrate ion-radical. Further reactions include the generation of a radical that interacts with the second molecule of the reactant. The product of this step is in the ion-radical form, and it starts another cycle of the substrate conversion in the newly formed ion-radical at the expense of electron transfer.

Two general advantages of photoinduced redox processes deserve to be emphasized. First, they can be carried out in neat organic solvents not requiring the use of a conducting salt as in electrochemistry and not encountering the problems of limited solubility of the salts in aprotic (organic) solvents. Second, the active redox reactant/reagent is in the excited state formed by light absorption and present at a very low steady-state concentration; this avoids competition with overreduction or overoxidation. The latter is an understandable problem when the ion-radicals are formed in the vicinity of an electrode or in the presence of a significant concentration of the inorganic redox agent.

Attempts to use a heterogeneous rather than a homogeneous sensitizer in photochemical stimulation of ion-radical reactions are relevant. Sensitizers can be used as such or as covalently linked to the surface of silica beads. Supported photosensitizers used as a suspension in liquid offer obvious advantages: Relief in the separation of photoproducts, simplicity of analysis, recycling of the sensitizer, and circumventing of poor solubility in the reaction medium. As an example, the photoreactive deprotection of sulfonamides proceeds smoothly with the participation of the immobilized sensitizer 4-methoxynaphthol covalently grafted on silica. The sensitizer was filtered, washed, and successfully recycled after the reaction. The efficiency of the grafted sensitizer remained unchanged (Ayadim et al. 1999). Albini and Spreti (1986) employed a polymer that contained a chromophore. Fox (1991) used a sensitizer placed on a semiconductor surface. An attempt to use solar light rather than excitation by the help of special lamps is also worth mentioning (Cermenati et al. 1998).

One important discrepancy should be noted between photochemical and chemical ion-radical reactions. In the photochemical mode, an oxidized donor and a reduced acceptor remain in the same cage of a solvent and can interact instantly. In the chemical mode, these initial products of electron transfer can come apart and react in the bulk solvent separately. For example, one-electron oxidation of phenylbenzyl sulfide results in the formation of cation-radical both in the photoinduced reaction with nitromethane and during treatment with ammoniumyl species. Sulfide cation-radicals undergo fragmentation in the chemical process. Cage effect is operable in the photochemical reaction: The phenylbenzyl sulfide cation-radicals are formed and instantly react with the donor (nitromethane) molecules giving rise to phenylbenzyl sulfoxide. As for the ammoniumyl reaction, the sulfide cation-radicals react as the separated species undergoing fragmentation and then oxidation (Adam et al. 1998).

Here is another example: The "normal" electrochemical reduction of 4-nitrobenzyl thiocyanate leads to the 4-nitrobenzyl radical and thiocyanate. The only products are 4,4′-dinitrobibenzyl and 4-nitrotoluene arising from the 4-nitrobenzyl radical (Bartak et al. 1971):

$$4\text{-}O_2NC_6H_4CH_2SCN + e \rightarrow (4\text{-}O_2NC_6H_4CH_2SCN)^{-\bullet} \rightarrow 4\text{-}O_2NC_6H_4CH_2^{\bullet} + {}^{-}SCN$$

$$\tfrac{1}{2}\,4\text{-}O_2NC_6H_4CH_2CH_2C_6H_4NO_2\text{-}4' \leftarrow 4\text{-}O_2NC_6H_4CH_2^{\bullet} \rightarrow 4\text{-}O_2NC_6H_4CH_3$$

Photoinduced electron transfer in the presence of a sensitizer (9,10-diphenylanthracene) also generates the same anion-radical. However, its disintegration proceeds within the solvent (acetonitrile) cage. Inside the cage, the 4-nitrobenzyl radical and thiocyanate ion unite anew, but in this case, by their soft-to-soft ends. This nucleophilic reaction takes place faster than the back electron transfer does. The final, stable product of the whole process is 4-nitrobenzyl-*iso*-thiocyanate (Wakamatsu et al. 2000):

$$4\text{-}O_2NC_6H_4CH_2SCN + e \rightarrow (4\text{-}O_2NC_6H_4CH_2SCN)^{-\bullet} \rightarrow \{4\text{-}O_2NC_6H_4CH_2^{\bullet} \cdots {}^{-}SCN\} \rightarrow$$

$$\rightarrow \{4\text{-}O_2NC_6H_4CH_2^{\bullet} \cdots {}^{-}NCS\} \rightarrow 4\text{-}O_2NC_6H_4CH_2NCS + e$$

One principally different method of photoexcitation consists in the so-called two-color, two-laser flash photolysis. This method allows exciting ion-radicals already generated during the first laser (first color) flash photolysis. With a short-time delay after the first laser flash, the ion-radicals are selectively excited by the second laser (second color) flash. This flash is of the wavelength tuned to the absorption of the ion-radical initially formed. As a result, the ion-radical transforms into

the excited state and enhances its reactivity. Thus, the biologically important one-electron oxidation of alcohols is hard-to-reach in modeling studies because of their high oxidation potential. The two-color, two-laser flash photolysis provides such a possibility. Cai et al. (2007) performed the one-electron oxidation of methanol, ethanol, or iso-propanol employing the trimethoxybenzene cation-radical ($TMB^{+\bullet}$) in the excited state ($TMB^{+\bullet}$*). $TMB^{+\bullet}$ was formed by the photoinduced bimolecular electron-transfer reaction from TMB to chloranil during the first 355 nm laser flash photolysis. Then, $TMB^{+\bullet}$* was generated from the selective excitation of $TMB^{+\bullet}$ during the second 532 nm laser flash photolysis. $TMB^{+\bullet}$* is able to take one electron from an alcohol. The resulting alcohol cation-radical gives its hydroxyl proton to the chloranil anion-radical and transforms into the corresponding aldehyde. The latter transformation is just the same physiological reaction that is desirable to be monitored.

5.2.2 Effect of Electric Field

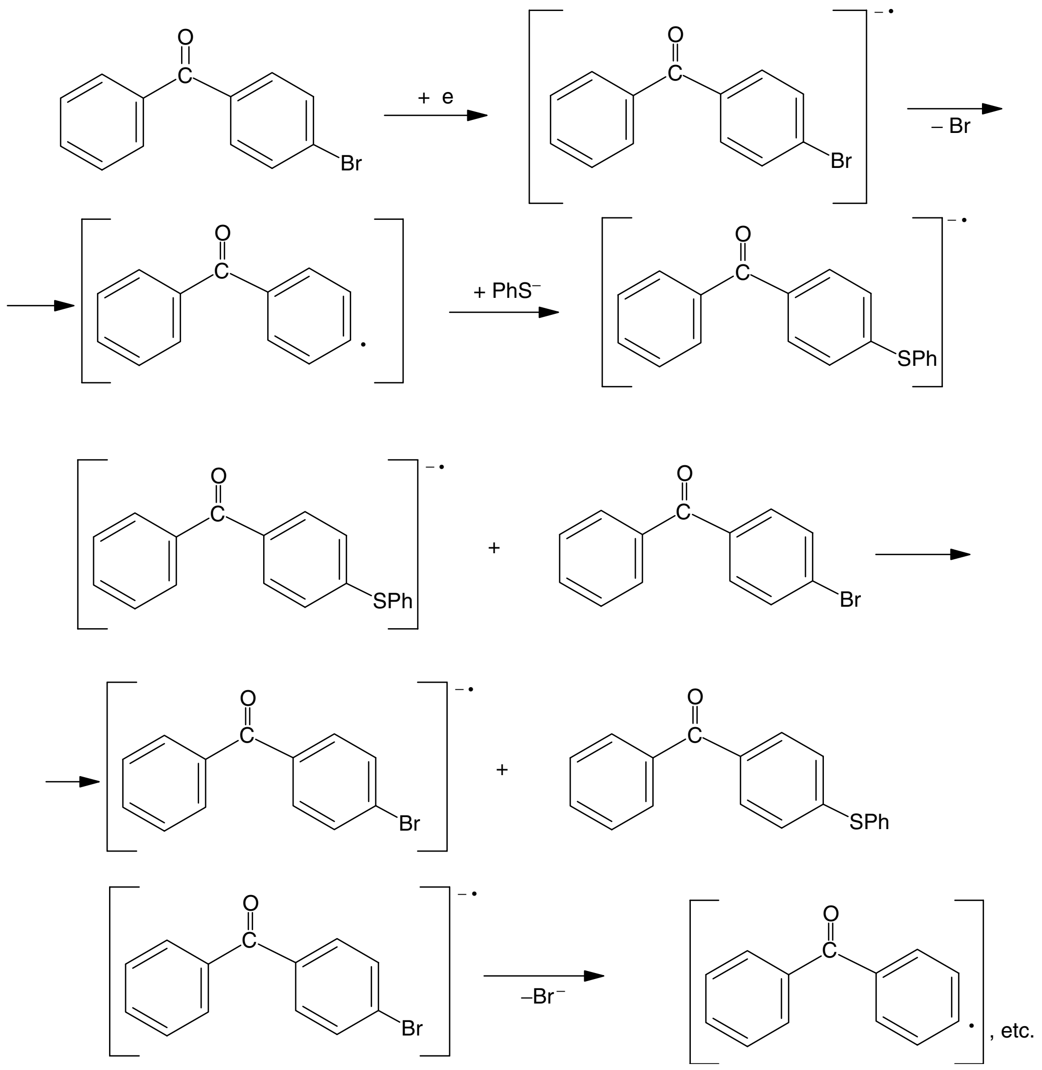
Certain ion-radical reactions can be stimulated by means of direct potential imposition without mediators. In these reactions, the substrate is a depolarizer, and the reactant is a conducting electrolyte. Electrochemical organic synthesis is a well-developed field, and many relevant examples have been provided in all the chapters of this book. Now it is reasonable to give only the significant examples.

Thus, thioarylation may be facilitated electrochemically. The conventional nucleophilic substitution of the phenylthio group for bromine in 4-bromobenzophenone requires extremely rigid conditions. When a difference in electric potentials is set up, the reaction proceeds readily and gives products in a high yield (80%). It is sufficient to set up only the potential difference necessary to ensure the formation of the substrate anion-radical (with the potential and current strictly controlled). The chemical reaction takes place in the bulk of solution and yields 4-(phenylthio)benzophenone (Pinson and Saveant 1974) (Scheme 5.1).

1-Bromonaphthalene does not react with benzenethiol (thiophenol) salts. However, if electric current is passed through a solution containing 1-bromonaphthalene, the tetrabutylammonium salt of thiophenol, and DMSO, then 1-(phenylthio)naphthalene is produced in 60% yield. When the reaction is conducted in acetonitrile, it leads to naphthalene above all (Pinson and Saveant 1978, Saveant 1980, Amatore et al. 1982). In the electrochemically provoked reaction, it is sufficient to set up the potential difference corresponding to the initial current of the reduction wave to transform 1-bromonaphtahalene into 1-naphthyl radical. The difference in the consumption of electricity is rather remarkable: In the absence of thiophenolate, bromonaphthalene is reduced, accepting two electrons per molecule; in the presence of thiophenolate, 1-bromonaphthalene is reduced accepting two electrons for every ten molecules. The reaction with the thiophenolate ion is catalyzed by electric current and takes a reaction path shown in Scheme 5.2.

The reaction in Scheme 5.2 proceeds through the formation of the 1-bromonaphthalene anion-radical, which rapidly converts into the naphthyl radical. Thiophenolate intercepts the naphthyl radical and forms the anion-radical of 1-(phenylthio)naphthalene. The reaction takes place in the preelectrode space. It competes with the formation of the unsubstituted naphthalene. The debromination is a result of hydrogen abstraction from the solvent SolH by the naphthyl radical. The unreacted 1-bromonapthalene oxidizes the 1-(phenylthio)naphthalene anion-radical formed. This leads to the neutral 1-(phenylthio)naphthalene and the anion-radical of 1-bromonaphthalene. The reaction takes place in the bulk solution and is the key-point for the chain propagation.

Instead of bromobenzophenone (see Scheme 5.1), 4-bromobenzonitrile may also be used as a substrate (Pinson and Saveant 1978). The latter two compounds carry not only bromine, but also other electrochemically active groups, that is, C=O or C≡N. These groups do not inhibit the substitution. Along with the thiophenyl, the thiomethyl or thio-*tert*-butyl groups can be introduced as substituting fragments. The yields of the substitution products are high (from 60 to 95%), and one electron is consumed for every 20–30 molecules of substrate. The reactions proceed at an ambient temperature and do not take place when a potential difference is not set up.

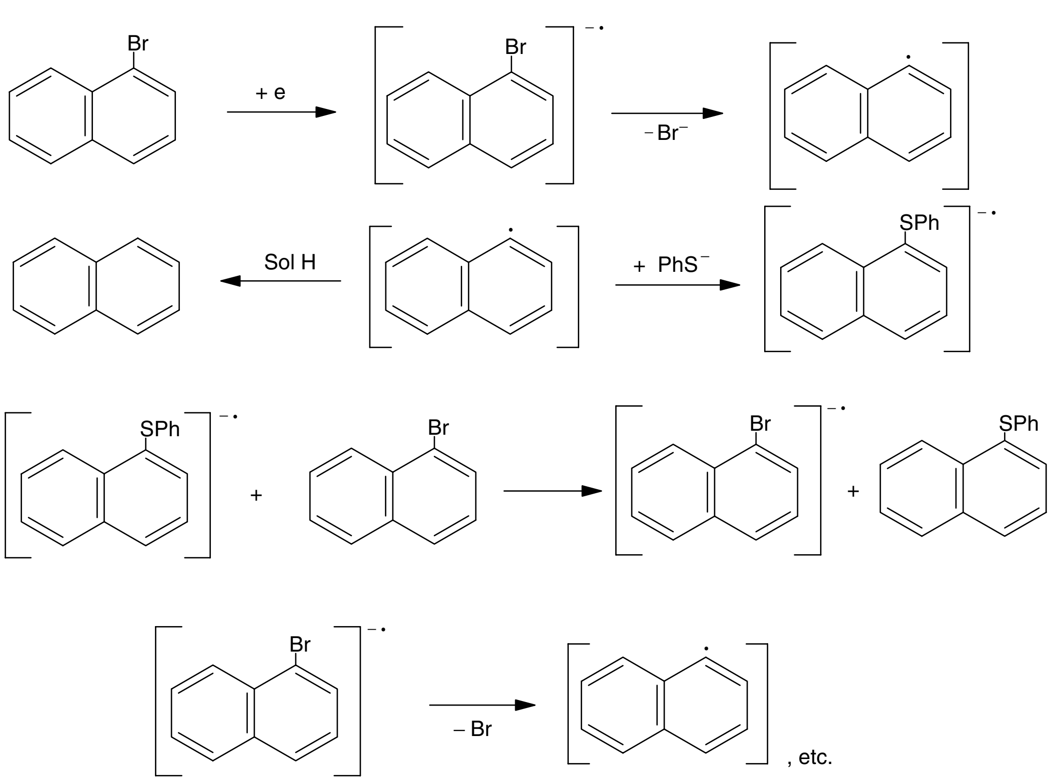


SCHEME 5.1

The effect of electric current has the following features:

1. The reactions are selective and give products in high yields. The replacement of a leaving group needs no activation of a substrate by electron-accepting substituents.
2. The starting compounds have a greater electron affinity than the substitution products. Therefore, the substrate easily accepts an unpaired electron belonging to the product anion-radical. This creates conditions necessary for the development of the chain process, and the reaction becomes catalytic with respect to the current passed.
3. Such an electrode potential should be chosen that initiates the substrate substitution without reducing the product of substitution.

The method of electrochemical initiation of these reactions has some limitations, the main limitation being that the probability of substitution of a leaving group by a nucleophile depends on the nature of the substrate. Let us compare two reactions similar in the solvent employed (DMSO) and the nucleophile used (Bu_4NSPh), but different in the chosen substrates (4-bromobenzophenone or bromobenzene)



SCHEME 5.2

(Pinson and Saveant 1978, Swartz and Stenzel 1984). On electrochemical initiation (Hg cathode), 4-bromobenzophenone gives rise to 4-(phenylthio)benzophenone in the 80% yield, whereas bromobenzene yields diphenyldisulfide with the yield of only 10% and unsubstituted benzene with the yield of more than 95%. In the bromobenzene case, this means that the substitution is a minor reaction, whereas the main route is ordinary debromination. According to Swartz and Stenzel (1984), the substrate anion-radicals are initially formed in the preelectrode space. Stability of these anion-radicals are different. The less stable anion-radicals of bromobenzene do not have enough time to go into the catholyte pool. They give rise to the phenyl radicals in the vicinity of the cathode. The phenyl radicals are instantly reduced into the phenyl anions. They tear protons from the solvent and yield benzene.

The much steadier anion-radicals of 4-bromobenzophenone are able to diffuse into the volume without disintegration. In the volume, they lose the bromine anion and form the corresponding radicals, which are intercepted with the thiophenolate anions. The product of so-to-speak nucleophilic substitution is formed.

Swartz and Stenzel (1984) proposed an approach to widen the applicability of the cathode initiation of the nucleophilic substitution, by using a catalyst to facilitate one-electron transfer. Thus, in the presence of PhCN, the cathode-initiated reaction between PhBr and Bu_4NSPh leads to diphenydisulfide in such a manner that the yield increases from 10 to 70%. Benzonitrile captures an electron and diffuses into the pool where it meets bromobenzene. The latter is converted into the anion-radical. The next reaction consists of the generation of the phenyl radical, with the elimination of the bromide ion. Since generation of the phenyl radical takes place far from the electrode, this radical is attacked with the anion of thiophenol faster than it is reduced to the phenyl anion. As a result, instead of debromination, substitution develops in its chain variant. In other words, the problem is to choose a catalyst such that it would be reduced more easily than a substrate. Of course, the catalyst anion-radical should not decay spontaneously in a solution.

The rate of an electron transfer from the reduced catalyst to the substrate is also important. If the rate is excessively high, the electron exchange will occur within the preelectrode space and the catalytic effect will not be achieved. If the rate is excessively low, a very high concentration of the catalyst will be needed. However, at high concentration, the anion-radicals of the catalyst will reduce the phenyl radicals. Naturally, this will be unfavorable for the chain process of the substitution. As catalysts, substances that can be reduced at potentials by 50 mV less negative than those of the substrates should be chosen. The optimal concentration of the catalyst must be an order lower than that of a substrate (Swartz and Stenzel 1984).

The naphthalene is apparently very good at mediation. Electrochemical reduction of naphthalene generates the anion-radical of specific reduction power. For instance, it is capable of transforming the platinum metal to the negative oxidation state; the process details were described in a recent work by Ghilane et al. (2007). It is practically important that such a change of the platinum nature results in transition of the conducting metal into an insulating material.

5.2.3 Effect of Magnetic Field

The effect of a magnetic field on the rate of ion-radical reactions has a physical background (Buchachenko 1976, Salikhov 1996). A magnetic field effect is basically interplay between spin dynamics and diffusion dynamics. The effect of a magnetic field on the processes involving spin particles has been thoroughly discussed (Sagdeev et al. 1977, Rodgers et al. 2007). The enforcement of the strength of the earth's magnetic field, 0.398 A · cm^{-1} or 0.5 Oe to 15,920 A · cm^{-1} (20,000 Oe), considerably changes the ratio of products resulting from the interaction of pentafluorobenzyl chloride with *n*-butyl lithium; in high magnetic fields, the yield of a substitution product, namely, *n*-pentylpentafluorobenzene, rises significantly. The whole set of products obtained can be seen from the following system of equations:

$$C_6F_5CH_2Cl + BuLi \rightarrow [(C_6F_5CH_2Cl)^{-\bullet}]Li^+ + Bu^\bullet$$

$$[(C_6F_5CH_2Cl)^{-\bullet}]Li^+ \rightarrow C_6F_5CH_2^\bullet + LiCl$$

$$C_6F_5CH_2^\bullet + {}^\bullet H_2CC_6F_5 \rightarrow C_6F_5CH_2CH_2C_6F_5$$

$$Bu^\bullet + Bu^\bullet \rightarrow Bu\text{–}Bu$$

$$C_6F_5CH_2^\bullet + Bu^\bullet \rightarrow C_6F_5CH_2Bu$$

Obviously, the reaction leading to the substitution product is of the following chain nature:

$$C_6F_5CH_2^\bullet + BuLi \rightarrow [(C_6F_5CH_2Bu)^{-\bullet}]Li^+$$

$$[(C_6F_5CH_2Bu)^{-\bullet}]Li^+ + C_6F_5CH_2Cl \rightarrow [(C_6F_5CH_2Cl)^{-\bullet}]Li^+ + C_6F_5CH_2Bu, \text{ etc.}$$

Sensitivity to the magnetic field strength has also been observed in the process of photoisomerization of *trans*-stilbene (*t*S) into *cis*-stilbene (*c*St) in the presence of pyrene (P). The reaction was run in a solution with acetonitrile, DMSO, or hexafluorobenzene being a solvent. During the reaction, spin polarization was established (Lyoshina et al. 1980). The spin polarization was explained by the following sequence of the elementary acts:

$$tS + P + h\nu \rightarrow tS + P^S{}_1 \rightarrow (tS)^{-\bullet} + (P^{+\bullet})^S \rightarrow (tS)^{-\bullet} + (P^{+\bullet})^T \rightarrow (tS + P^T) + (cS + P)$$

According to this sequence, formation of *cis*- and *trans*-stilbenes is preceded by formation of a magnetosensitive ion-radical by a singlet-triplet conversion. This means that spin polarization must be observed in *cis*- and *trans*-stilbene, and the isomerization rate must depend on the intensity of the magnetic field. These predictions were confirmed experimentally (Lyoshina et al. 1980). Hence, the ion-radical route for trans → cis conversion is the main one under photoirradiation conditions. Until now, the mechanisms assumed for such processes have involved energy transfer and did not take into account single-electron transfer. The electron transfer takes place in reality and makes the

whole process energetically more favorable. It is worth noting that a confined system is necessary for a radical pair during the singlet-triplet spin conversion. The influence of the medium viscosity and medium-cage effects on this conversion is discussed in this chapter. Special experiments revealed that the medium-cage or micellar effect is more important than viscosity (Wakasa 2007).

Many organic ion-radical reactions are initiated electrochemically. Reports from several laboratories have demonstrated that magnetic forces, generated by the interaction of an external field with current-carrying ions or with redox molecules that possess large intrinsic magnetic moments, can lead to significant increases in the rate of the electrochemical reaction. For example, the transport of a paramagnetic ion away from the electrode surface is greatly facilitated by an externally applied nonuniform magnetic field. The magnetic-field effect results in current enhancements as large as 400% at disk-shaped platinum microelectrodes. In contrast, experiments have been reported in which a nonuniform magnetic field generated internally by magnetization of the disk-shaped iron or nickel microelectrodes was used to focus electrochemically generated ion-radicals toward the electrode surface. In particular, a magnetic-field effect has been demonstrated on the freedom of diffusion of the nitrobenzene anion-radical generated electrochemically (Grant et al. 1999, and references therein). A uniform magnetic field of 1 T (generated by an external electromagnet) was applied orthogonally to the exposed surface of the microelectrode, resulting in the magnetization of ferromagnetic (iron, nickel) material. The ion-radical, originating near the electrode, possesses a magnetic dipole moment. The redox reaction creates a thin layer in the electrode vicinity. The thin layer has a volume magnetic susceptibility greater than that of the bulk solution. Paramagnetic species have a strong tendency to move toward a region of higher magnetic field (Griffiths 1999). If the magnetic force is large enough to overcome thermal diffusion, then the ion-radical will be effectively "trapped" at the electrode surface. The proof-of-concept experiment described suggests that magnetic forces can be employed to control the spatial position of redox molecules in electrochemical cells.

Lioubashevski et al. (2007) proposed a quantitative model that accounts for the magnetic field effect on electrochemical reactions at planar electrode surfaces, with the uniform or nonuniform field being perpendicular to the surface. The model couples the thickness of the diffusion boundary layer, resulting from the electrochemical process, with the convective hydrodynamic flow of the solution at the electrode interface induced by the magnetic field as a result of the magnetic force action. The model can serve as a background for future development of the problem.

The concept of electromagnetic electron-transfer acceleration is being discussed increasingly with respect to biochemical reactions. Thus, electromagnetic-field activation of genes and the synthesis of stress proteins are supposedly initiated through the magnetic effect on moving electrons in DNA. This idea is supported by studies showing that the magnetic fields increase electron-transfer rates in cytochrom oxidase. Electromagnetic fields accelerate electron transfer and appear to compete with the intrinsic chemical forces driving the reactions. The "moving-charge interaction" model provides a reasonable explanation of these effects (Blank and Soo 2001).

Contributing almost nothing to chemical energy and being negligibly small (and traditionally ignorable), magnetic interactions are the only ones, which are able to change electron spin of reactants and switch over the reaction between spin-allowed and spin-forbidden channels. Ultimately, they indeed control chemical reactivity and biological processes (Buchachenko 2001). Thus, the production of adenosine triphosphate (ATP) in mitochondria depends on the magnesium nuclear spin and magnetic moment of Mg^{2+} in creatine kinase and ATPase. Enzymic synthesis of ATP is an ion-radical process. Ion-radical pair (IRP) recombination is the force field of this synthesis. Magnetic and microwave fields control the spin state (singlet or triplet) of the pairs and affect spin selectivity and the very course of the biochemical transformation in total (Buchachenko et al. 2006).

5.2.4 Effect of Microwave Field

Let us compare behavior of water and 1,4-dioxane in the microwave field. Their boiling temperatures are 100 and 101°C, respectively. Under conditions of a 150 W microwave irradiation in a

hermetic vessel for 30 s, water is heated up to 120°C, although the dioxane temperature remains unchanged (Lidstrom et al. 2001). Water is a liquid with a large dipole moment, whereas the dipole moment of dioxane is zero. The external microwave field brings about the dipole align by the molecule rotation. It is the applied field that provides the energy for this rotation. The field oscillates and the rotation takes on the vibratory character. The vibratory rotation eventually results in swift elevation of the sample temperature. Importantly, the oscillation frequency must be in the middle region. Under the influence of a high-frequency field, the dipoles do not have sufficient time to respond to the oscillating field and, therefore, do not rotate. Since no motion is induced in the molecules, no energy transfer takes place and therefore no heating occurs. Under low-frequency irradiation, the molecule rotates in phase with the oscillating field. The molecule gains some energy in this case, but the overall heating effect by this full alignment is small. In the middle region of frequencies, the dipole must have enough time to rotate and is in a phase difference between the orientation of the field and that of the dipole. This phase difference causes energy to be lost from the dipole by molecular friction and collisions, giving rise to dielectric heating. Thus, in the initial example, it becomes clear why 1,4-dioxane, which lacks the dipole characteristics necessary for microwave dielectric heating, does not get warm. Quite the reverse—water, which has a large dipole moment, readily warms up.

Dipole-moment bearing participants are common for organic ion-radical reactions. Naturally, microwave effect is applicable to them. Thus, Njoya et al. (2003) described a highly efficient microwave-induced procedure for preparation of various benzothiazole derivatives based on 2-chloromethyl-6-nitrobenzothiazole and lithium organics as starting materials. The reaction between them is completed in several minutes and consists of the replacement of chlorine by the corresponding organic fragment from the lithium reactant. The ion-radical mechanism of the replacement was confirmed by inhibition studies. Yields of the products were high enough (from 70 to 95%); the substances obtained are of biomedical importance. The review by Gellis et al. (2002) gives other convincing examples of useful microwave effects on electron-transfer reactions.

In microwave-assisted synthesis, a homogeneous mixture is preferred to obtain a uniform heating pattern. For this reason, silica gel is used for solvent-free (open-vessel) reactions or, in sealed containers, dipolar solvents of the DMSO type. Welton (1999), in a review, recommends ionic liquids as novel alternatives to the dipolar solvents. Ionic liquids are environmentally friendly and recyclable. They have excellent dielectric properties and absorb microwave irradiation in a very effective manner. They exhibit a very low vapor pressure that is not seriously enhanced during microwave heating. This makes the process not so dangerous as compared to conventional dipolar solvents. The polar participants of organic ion-radical reactions are perfectly soluble in polar ionic liquids.

At the same time, electrode-assisted ion-radical reactions can be seriously facilitated by the microwave irradiation. Earlier, we had already considered the ion-radical mechanism of dehalogenation of aromatic haloderivatives. Halonitrobenzenes transform into nitrobenzene much more easily when the microwave irradiation is applied during their reduction at small electrodes (Tsai et al. 2002). The effect was observed in the microwave-absorbing DMF solution. The authors suggest the formation of a "hot spot" region in the vicinity of the electrode surface. Under these conditions, dehalogenation (the chemical reaction) is affected more strongly than the mass-transport (the physical phenomenon). So, environmentally important processes of dehalogenation and detoxification of industrial halogenated compounds can be intensified by the combination of electroreduction with microwave irradiation.

5.2.5 Effect of Acoustic Field

The ultrasonic irradiation of a solution induces acoustic cavitation, a transient process that promotes chemical activity. Acoustic cavitation is generated by the growth of preexisting nuclei during the alternating expansion and compression cycles of ultrasonic waves. For example, in aqueous liquid, temperatures as high as 4300 K and pressures over 1000 atm are estimated to exist within

each gas- and vapor-filled microbubble following an adiabatic collapse (Didenko et al. 1999). It is worthwhile noting that sonochemical reactions are accelerated if the reaction mass is cooled before and during sonication because cavitation increases under these conditions. However, this cannot be indefinitely continued as solvent viscosity limits the cavitation of the fluid as well as the propagation of sonic waves (Mason 1991).

If the yield of a silent reaction is *n%* after a specific period of time, whereas the yield of the corresponding sonochemical reaction is *m%*, the ratio *m/n* higher than 1 is described as the effect of ultrasound. The common opinion is that ultrasound effects originate from the general phenomenon of cavitation, which generates high temperatures, pressures, and shock waves. According to the hot spot theory (Neppiras and Noltingk 1950), the homogeneous ultrasound reaction takes place in the collapsing cavitation bubble and in the superheated (ca. 2000 K) liquid shell around it. Species with sufficient vapor pressure diffuse into the cavity where they undergo the effect of adiabatic collapse.

However, this commonly accepted theory is incomplete and applies with much difficulty to systems involving nonvolatile substances. The most relevant example is metals. For a heterogeneous system, only the mechanical effects of acoustic waves govern the sonochemical processes. Such an effect as agitation, or "cleaning" of a solid surface, has the mechanical nature. Ultrasound transforms potassium into its dispersed form. This transformation is favorable for an electron transfer from the metal to organic acceptor (see Chapter 2). Of course, ultrasonic waves interact with the metal by their cavitational effects. Electron-transfer reactions with participating metal particles and electroactive (polar) substrates proceed on the phase interface. Galiakhmetov and Smorodov (2002) assume that acoustic vibrations induce dipole moments on the polar substrates. The further development of the phenomenon resembles the situation considered for the microwave effect (see Section 5.2.4). Orientational relaxation of the dipole molecules on metal surface leads to release of the energy acquired. This accelerates the reaction. The authors propose the same approach to the reactions between organic donors and acceptors taking into account that the orientational relaxation proceeds at boundary surface of the cavitational bubbles.

It seems reasonable to note that the micro-jet stream generated by the ultrasonic cavitation promotes mass transport. Such an effect was discussed for proton transport in aqueous solutions (Atobe et al. 1999). Understandably, a proton moves in the solution as a hydrated particle. Nevertheless, we should pay attention on the similarity between proton and electron, in the sense that both are essentially quantum particles. A solvated electron, therefore, can be considered as a species that is similar to a hydrated proton. Hence, the micro-jet stream can promote electron transfer.

Stripping of an electron from the metal surface and electron transfer from the HOMO belonging to an organic donor are similar phenomena. It is significant that sonication promotes electron-transfer reactions, whereas ionic processes are essentially insensitive to cavitational phenomena (Luche et al. 1990). Ionic species are not produced by ultrasound. By and large, sonochemical reactions, either homogeneous or heterogeneous, correspond to processes in which the production of the reactive intermediate, an ion-radical or a radical, is stimulated by ultrasound effects. Although a complete physical explanation of such stimulation has not been elaborated yet, there is a set of ultrasonically influenced reactions. The following examples illustrate several principal manifestations of the ultrasonic effect.

Sonolysis provokes electron-transfer reactions in which hindered phenols act as donors (Aleksandrov et al. 1995). Steric hindrance does not allow a donor and an acceptor to come closer and thus, prevents or significantly hampers overlapping of the corresponding orbitals. Acoustic field effect helps in overcoming this hindrance.

Russell and Danen (1968) studied the sonication effect on the reaction between the lithium salt of 2-nitropropane and 4-nitrobenzyl bromide. A dual mechanism, ionic and ion-radical, characterizes this reaction. The ionic mechanism leads to the *O*-alkylation product and, eventually, to 4-nitrobenzaldehyde:

$$Me_2C{=}NOOLi + BrCH_2C_6H_4NO_2\text{-}4 \rightarrow LiBr + Me_2C{=}N(O){-}OCH_2C_6H_4NO_2\text{-}4$$

$$Me_2C{=}N(O){-}OCH_2C_6H_4NO_2\text{-}4 \rightarrow Me_2C{=}NOH + O{=}CHC_6H_4NO_2\text{-}4$$

The ion-radical route leads to the C-alkylated product, namely, 2-(4-nitrobenzyl)-2-nitro propane:

$$Me_2C{=}NOOLi + 4\text{-}O_2NC_6H_4CH_2Br \rightarrow Me_2CNO_2 + [(4\text{-}O_2NC_6H_4CH_2Br)^{-\bullet}]Li^+$$

$$[(4\text{-}O_2NC_6H_4CH_2Br)^{-\bullet}]Li^+ \rightarrow LiBr + [4\text{-}O_2NC_6H_4CH_2^{\bullet}]$$

$$[4\text{-}O_2NC_6H_4CH_2^{\bullet}] + Me_2C{=}NOOLi \rightarrow \{[4\text{-}O_2NC_6H_4CH_2C(Me_2)NO_2]^{-\bullet}\}Li^+$$

$$\{[4\text{-}O_2NC_6H_4CH_2C(Me_2)NO_2]^{-\bullet}\}Li^+ + 4\text{-}O_2NC_6H_4CH_2Br \rightarrow$$

$$\rightarrow LiBr + [4\text{-}O_2NC_6H_4CH_2^{\bullet}] + 4\text{-}O_2NC_6H_4CH_2C(Me_2)NO_2$$

$$[4\text{-}O_2NC_6H_4CH_2^{\bullet}] + Me_2C{=}NOOLi \rightarrow \{[4\text{-}O_2NC_6H_4CH_2C(Me_2)NO_2]^{-\bullet}\}Li^+, \text{ etc.}$$

Experiments in deoxygenated ethanol solution in the dark showed that, by stirring, 4-nitrobenzaldehyde is obtained in 60% yield, accompanied by 13% 2-(4-nitrobenzyl)-2-nitropropane. Under the same conditions, but with sonication, the yields are 23% of 4-nitrobenzaldehyde and 48% of 2-(4-nitrobenzyl)-2-nitropropane (Einhorn et al. 1990). The importance of this result consists in the following conclusion: The ultrasonic irradiation has a marked influence on the relative rates of the competing reactions and stimulates just the ion-radical one.

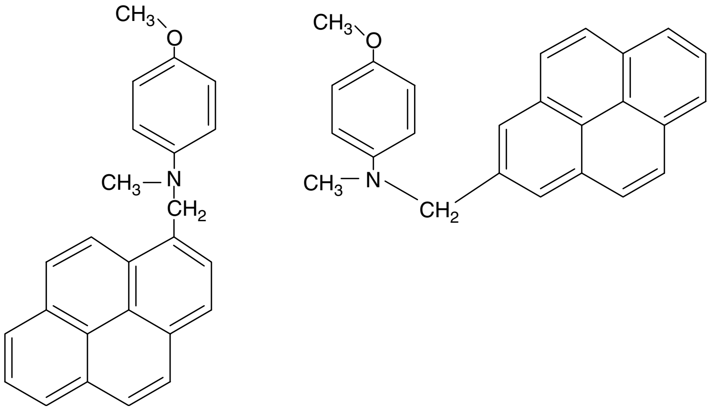
Romanian scientists compared one-electron transfer reactions from triphenylmethyl or 2-methyl benzoyl chloride to nitrobenzene in thermal (210°C) conditions and on ultrasonic stimulation at 50°C (Iancu et al. 1992, Vinatoru et al. 1994, Chivu et al. 2006). In the first step, the chloride cation-radical and the nitrobenzene anion-radicals are formed. In the thermal and acoustic variants, the reactions lead to the same set of products with one important exception: The thermal reaction results in the formation of HCl, whereas ultrasonic stimulation results in Cl_2 evolution. At present, it is difficult to elucidate the mechanisms behind these two reactions. As an important conclusion, the sonochemical process goes through the inner-sphere electron transfer. The outer-sphere electron transfer mechanism is operative in the thermally induced process.

According to Ando et al. (2000), the sonolytic acetoxylation of styrene by lead tetraacetate follows the ion-radical mechanism. Lead tetraacetate was not subject to the sonication influence. The ultrasonic effect facilitates electron transfer from styrene (the nonmetallic donor) to lead tetraacetate.

We cited a lot of examples when sonication accelerates ion-radical reactions. Logically, this effect might be considered as an independent diagnostic probe. However, this is not so. Thus, reaction of methyl vanillate with phenyliodonium bis(acetate) is initiated by ultrasonic irradiation and gives rise to the corresponding *o*-quinone monoketal, which is trapped by a series of furans. Monoadducts are formed and their formation is highly accelerated by the acoustic field. With no heating, these reactions are completed within 15–50 min. A thorough study showed that the acceleration is mainly caused by ultrasonic agitation, that is, by the effect of the mechanochemical nature. The system simply works as a perfectly stirred reactor with an enhanced mass transfer (compare the papers of Avalos et al. 2000, 2003).

5.2.6 Effect of Mechanical Action

This section considers initiation of organic ion-radical reactions by grinding, shearing, milling, and other kinds of mechanical actions. When relevant, practical applicability of the particular reactions is underlined. Readers interested in organic mechanochemistry as a branch of practical chemistry can be addressed to the corresponding monograph (Todres 2006). In mechanochemical reactions, formations of ion-radical states and CTCs (internal or intermolecular) are difficult to distinguish. However, charge transfer is essentially electron transfer. This is the main reason to consider here both the phenomena cojointly.



SCHEME 5.3

5.2.6.1 Mechanochromism

Conformational transitions and electron redistribution on pressure results in changes of the ion-radical properties and this is essential for optoelectronic devices. Pressure is the thrust distributed over a surface. The most important results of compression are reduction of molecular volumes and conformational changes of organic compounds. Spectral changes of solids are also termed "piezochromism." Let us consider several relevant examples of piezochromism.

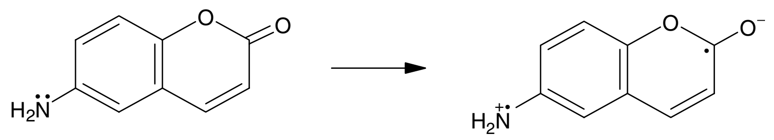
Two stable conformations of *N*-(1-pyrenylmethyl)-*N*-methyl-4-methoxyaniline, the linear and bent (V-like) forms are depicted in Scheme 5.3* (He et al. 2004).

Pressure provokes transition of the linear (extended) conformation into the bent (V-like) one. (The V-like form is more compact and occupies a smaller volume.) It is obvious that the V-like form is favorable in respect of intramolecular electron transfer from the donor (the aniline part) to the acceptor (the pyrene part). In the utmost level of the phenomenon, the donor part transforms into the cation-radical moiety, whereas the acceptor part passes into the anion-radical moiety. Such transformation is impossible in the case of the extended conformation because of the large distance between the donor and acceptor moieties. The spectral changes observed reflect this conformational transition at elevated pressures.

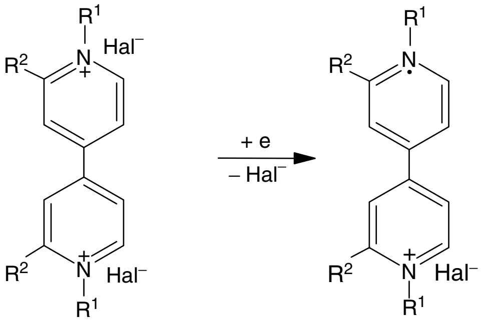
In the spectral sense, there are three emitting sources: (1) local excited state of the pyrene moiety, (2) intermolecular donor–acceptor complex, and (3) intramolecular electron-transfer compound. At normal pressure, the emission from the intermolecular complex is much larger than that from other sources. With the increase in pressure, the donor and acceptor moieties get much closer, and the emission of the intermolecular complex shifts greatly to the red side, the relative efficiency drops significantly. Meanwhile, the emission from the intramolecular electron-transfer compound increases with the surrounding pressure, and fluorescence efficiency becomes relatively higher. At higher pressure, the intermolecular and intramolecular complexes exist simultaneously, but their emission is observed at significantly different wavelength ranges. The emission generated by the intramolecular electron transfer is enhanced by the increase in pressure (He et al. 2004).

A recent review (Todres 2004) gives a number of examples when pressure enhances light emission from photoexcited organic compounds. Here, however, one case will be considered of pressure-weakening luminescence intensity. An exception sometimes helps understanding the regularity better. Photoexcitation of 6-aminocoumarin induces intramolecular electron transfer. The phenomenon, in its utmost form, is represented by Scheme 5.4. The amino group can rotate, giving rise to the twisted conformation. With respect to nitrogen of the amino group, sp^2 planar hybridization can be changed by sp^3 pyramidal hybridization on excitation. In any case, two excited states,

* Schemes 5.3–5.5 and Section 5.2.6.2 have been taken from Todres, Z.V., *Organic Mechanochemistry and Its Practical Applications*, Taylor and Francis, Boca Raton, FL, 2006. With permission.



SCHEME 5.4



R^1 = Me, R^2 = CN, Hal = Br; R^1 = Ph, R^2 = H, Hal = Cl;
R^1 = Me, R^2 = H, Hal = Cl

SCHEME 5.5

planar and twisted, are formed. As shown, just the twisted state is responsible for the luminescence of 6-aminocoumarin. Pressure leads to the loss in intensity of the emission. The loss with increasing pressure is explained by two reasons: a decrease in efficiency caused by an increased rate of non-radiative energy dissipation and a decrease in energy transfer caused by an increase in the energy barrier between the two excited states. As a result, the light emission falls when the pressure rises (Dadali et al. 1994, references therein) (Scheme 5.4).

When mechanical vibration of bis(pyridinium) salts (see Scheme 5.5) was conducted with a stainless steel ball in a stainless steel blender at room temperature under strict anaerobic conditions, the powdery white surface of the dicationic salts turned deep blue-purple (Kuzuya et al. 1993). Single-line ESR spectra were recorded in the resulting powder. No ESR spectra were observed in any of the dipyridinium salts when mechanical vibration was conducted with a Teflon-made ball in a Teflon-made blender under otherwise identical conditions. When observed, the ESR signals were quickly quenched on exposure to air and the starting dicationic salts were recovered. Each of the resulting powders was dissolved in air-free acetonitrile, and the ESR spectra of the solution were recorded after the material had been milled under anaerobic conditions. Analysis of the signal hyperfine structure confirmed the formation of the corresponding cation-radicals, which are depicted in Scheme 5.5.

An entering electron populates the lower vacant MO of the cation-radical and appears to be unpaired. With an unpaired electron, polarizability of a molecule increases and its excitation by light is facilitated. This enhances the intensity of light absorption and shifts it to the region of higher wavelengths. This kind of mechanochromism is caused by the emission of exoelectrons from a metal-abraded surface (the so-called Kramer effect, see Chapter 8).

5.2.6.2 Mechanopolymerization and Mechanolysis

This kind of polymerization is used for preparation of polymers for special applications. In the preparative scale, ion-radical mechanopolymerization is accompanied with mechanodepolymerization. Although the latter process does not always include the ion-radical stage, mechanopolymerization and mechanodepolymerization should be discussed cojointly.

Polymers can be made by vibromilling of some monomers with steel balls. No initiators are needed. Kramer effect, that is, the action of the electron stream developed by mechanoemission during vibratory milling initiates the polymerization. On vibratory milling, acryl and methacrylamides give anion-radicals, which are key species in the reaction (Simonescu et al. 1983):

$$CH_2{=}CRCONH_2 + e \rightarrow (CH_2{=}CRCONH_2)^{-\bullet}\ \{R{=}H, CH_3\}$$

$$(CH_2{=}CRCONH_2)^{-\bullet} + CH_2{=}CRCONH_2 \rightarrow {}^{-}CH_2{-}CH(CONH_2){-}CH_2{-}CR^{\bullet}{-}CONH_2$$

Further growth of the polymeric chain proceeds in the usual manner. Compared to the polymeric materials obtained by conventional methods, the mechanochemically synthesized polyacryl and polymethacrylamides have lower molecular weights (Simonescu et al. 1983). Acrylonitrile, styrene, ε-caprolactam, and isoprene as well as aryl and methacrylamides have special optimal duration of the polymerization on grinding (Oprea and Popa 1980). In the case of the aryl and methacrylamides, the polymerization proceeds slowly, usually between 24 and 72 h. After that, some acceleration takes place and the process is completed in 96 h (in total).

Chain growth is predominant at the beginning of the process, when mainly an unreacted monomer presents in the reaction medium and the synthesized polymers have not reached sufficient size ("critical length") to concentrate the mechanical energy. Molecular weight also increases near the maximum of the conversion, when most of the monomer is consumed during the acceleration period. When this maximum is reached, degradation takes effect and results in a decrease of molecular weight to a limiting value of 10^3–10^4. Hence, the fixed and even reduced molecular weight of polymers is the specific feature of such polymerization.

Mechanically initiated reactions can be used to create thermally stable polymer films. Such films form on various surface factors. They are very dense, although amorphous (Simonescu et al. 1983). The films are thermally and frictionally more stable than the thermally stable polymers obtained by conventional methods (Krasnov et al. 2002). The discussed case of polymerization can be of interest if amorphous polymers with moderate molecular weights are needed.

When polymerization proceeds in the presence of modifiers, the mechanochemical process enhances cross-linking and, correspondingly, improves the physicochemical properties of final plastics. For example, mechanochemical treatment of acrylonitrile butadiene styrene (ABS) plastic in the presence of toluene diisocyanate improves thermal oxidative stability of the plastic (Chetverikov et al. 2002).

So it is obvious that mechanical activation of monomers brings about two competitive processes: the growth of polymer chain and the chain destruction. A number of studies were undertaken to find optimal conditions regarding duration of the polymerization reaction, its temperature, allowed loading, and so on. Examples were presented in a review by Mit' et al. (2003).

Krasnov et al. (2003) gave a principal example of the combination of tribochemical and conventional methods for preparation of poly(peryleneimides) with improved properties. Polymers of this type are used in the manufacture of films for microelectronics. Conventionally, synthesis of such polymers is conducted in the chlorophenol–phenol mixture at a temperature exceeding 210°C, for 12 h. The solid-state polymerization of 4,4′-diaminodiphenyl oxide and perylene-3,4,9,10-tetracarboxylic dianhydride was mechanically initiated by grinding. To prevent destructive processes on prolonged grinding, the mechanochemical action was stopped after 40 min; after that, the reaction mass obtained was dissolved in liquid phenol and heated to 160°C for 16 h. The resulting polyimide showed perfect characteristics and, importantly, formed transparent bright red films. It was also demonstrated (Mit' et al. 2004) that the reaction between diaminodiphenyl oxide and pyromellite dianhidride led to oligomeric amidoacids with the molecular weight up to 2000 if the synthesis was carried out in a shear-type mixer using ethanol as a dispersing medium.

As already mentioned, mechanically induced polymerization is attended by depolymerization or mechanolysis. The term "mechanolysis" denotes bond scission under mechanical activation. Such kind of bond scission is reversible in principle. Because mechanolysis results in formation of radicals, it

should be classed with homolytic reactions also named homolysis. As this homolysis takes place, the free radicals formed enter the usual free-radical reactions, namely, recombination, decomposition, addition, and substitution. However, the mechanically induced homolysis has some features. The implemented energy stretches the polymer backbone chain, which is then cleaved: R–R → [R···R•] → R• + R•. The radicals R• are removed from each other and leave the unit volume. The rupture of the junction bond is the limiting step of the reaction. The emergence of radicals from the cage of their incipiency proceeds with diffusion rates. Mechanical stress enhances the mobility of the reacting species. The formation of free space and creation of a favorable arrangement of radicals are crucial for radical recombination. The important specificity of mechanochemical (mostly solid phase) reactions consists of generating active species and ensuring mass transfer (to let reagents meet each other).

Two mechanisms of mechanochemical reactions are most likely. First, under the action of mechanical stress, intermixing occurs at the molecular level. Second, the product forms on the surface of macroscopic reacting species. Formed in the solid phase, the radicals generated recombine so that mechanolysis proceeds as a reversible reaction. However, the term "reversibility" should be applied only to the bond formation between radicals. For example, the structure of "recombined" product can be and is different from that of the starting material. It is the main feature that disturbs conventional reversibility of the radical recombination during mechanolysis.

Depolymerization of some natural polymers is another typical example. Milling of chitin or chitosan, at ambient temperature, leads to cleavage of the cellulose polymeric chain. Scission of 1,4-glucosidic bonds takes place, and the radicals formed recombine. Based on electron spin resonance, Sasai et al. (2004) monitored both the homolysis and the radical recombination. The recombination led to the formation of midsize polymeric chains only. Some balance was established between the homolytic depolymerization and the size-limited recombination of the radicals primarily formed.

At this point, it is useful to compare mechanochemical synthesis of polystyrene, poly(methyl methacrylate), and styrene-acrylonitrile copolymer in a vibratory mill and in an ultrasonic reactor (Boehme et al. 2003). A vibratory mill allows obtaining low-molar-mass polymers in a short time. However, the advantages of the mill are restricted because of the degradation of the polymers. To generate real macromolecules, the ultrasonic reactor is preferred. With all the vinyl polymers, the active terminal radicals pass into the more stable radicals keeping the free valence in the middle of the chain, thus forming chain radicals. The chain radicals lead to the degradation of the chain by forming C=C bonds:

$$-CH_2-\dot{C}H_2-\underset{\displaystyle R}{\underset{|}{C}H}-CH_2-CH_2- \longrightarrow -CH_2-CH_2=\underset{\displaystyle R}{\underset{|}{C}H}+{}^{\bullet}CH_2-CH_2-$$

According to the general rule of alkene chemistry, the unsaturated bonds are usually formed close to branches. On formation, the expelled radicals react with neighboring macromolecules abstracting a hydrogen atom from them. Such abstraction gives onset of chain degradation of polymers. Nevertheless, the number of macromolecules with double bonds is in fact 10^3 times higher than the number of free radicals in the less-stressed regions of the polymer after breaking of the chain reaction (Heinicke 1984).

For polymers, the relative rates of destruction are defined, first of all, by the rigidity of their structure. The rigidity increases on passing from flexible-chain polyethylene to more rigid polystyrene and then to polypeptides. Polypeptides possess special rigidity owing to the presence of peptide bonds in the backbone and a dense network of hydrogen bonds. The maximum destruction rates were detected for 3-D polymers such as glyceromaleate (Dubinskaya 1999). Because of the nonuniformity of the stress distribution inside the polymer, the overloaded bonds are first broken after the application of stress. An industrially important process of polymer modification can be realized in extruders. However, a type of the extruder has a marked influence on this process. For instance, it is impossible to obtain a cross-linked polyethylene with maleic anhydride in the usual extruders.

In this case, there are too few macroradicals available for reaction because of insufficient polymer degradation. In the disk-type extruder, a higher-stress gradient is achievable, more macroradicals are generated, and intensive cross-linking between polyethylene or highly chlorinated polyethylene and maleic anhydride or methyl methacrylate can be obtained (Heinicke 1984, Zhao et al. 2002, 2003).

During mechanolysis of poly(methylmethacrylate), the radical concentration gradually increased to a maximum and then gradually decreased (Kondo et al. 2004). It was suggested that the radical disproportionation or recombination progressed together with the radical formation. As with molecular mass of the starting polymer, it decreased exponentially toward the limiting value, and the limiting mass was larger with decreases in mechanical energy.

Carboxylated polymers can be prepared by mechanical treatment of frozen polymer solutions in acrylic acid (Heinicke 1984). The reaction mechanism is based on the initiation of polymerization of the frozen monomer by free macroradicals formed during mechanolysis of the starting polymer. Depending on the type of polymer, mixed, grafted, and block polymers with a linear or spatial structure are obtained. What is important is that the solid-phase reaction runs with a relatively high rate. For instance, in the polyamide reactive system with acrylic acid, the tribochemical reaction leading to the copolymer is completed after a treatment time of 60 s. As a rule, the mechanical activation of polymers is mainly carried out in a dry state, because the structural imperfections appear most likely here.

Tribochemistry was also applied as an economical method of rubber devulcanization. Devulcanization is the process of rupture, entirely or partially, of carbon–carbon, carbon–sulfur, or sulfur–sulfur bonds in the chemical network resulting from polymer cross-linking during rubber manufacturing. Each year, about 2 billion tires are discarded throughout the world, which represents a major loss of an important resource. Known methods of devulcanization involve high energy consumption, complicated equipment, toxic reagents, and toxic by-products produced, and eventually lead to compounds that are not industrially acceptable.

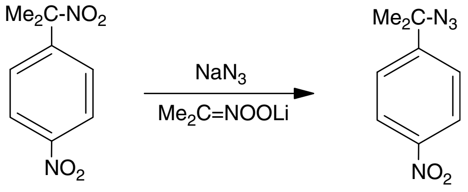
Mechanical grinding of rubber in the presence of a chemical additive brings about devulcanization to be economically profitable (Sangari et al. 2003). During mechanochemical treatment of rubber, the direct breakage of the carbon–carbon backbone chain takes place alongside the breakage of carbon–sulfur and sulfur–sulfur bonds. Free radicals form and recombine. Chemical additives are used to control the recombination. This provides compounds that can be molded and revulcanized within the conventional rubber manufacturing process. The revulcanized samples showed good mechanical properties for further industrial applications.

5.3 EFFECT OF CHEMICAL ADDITIVES

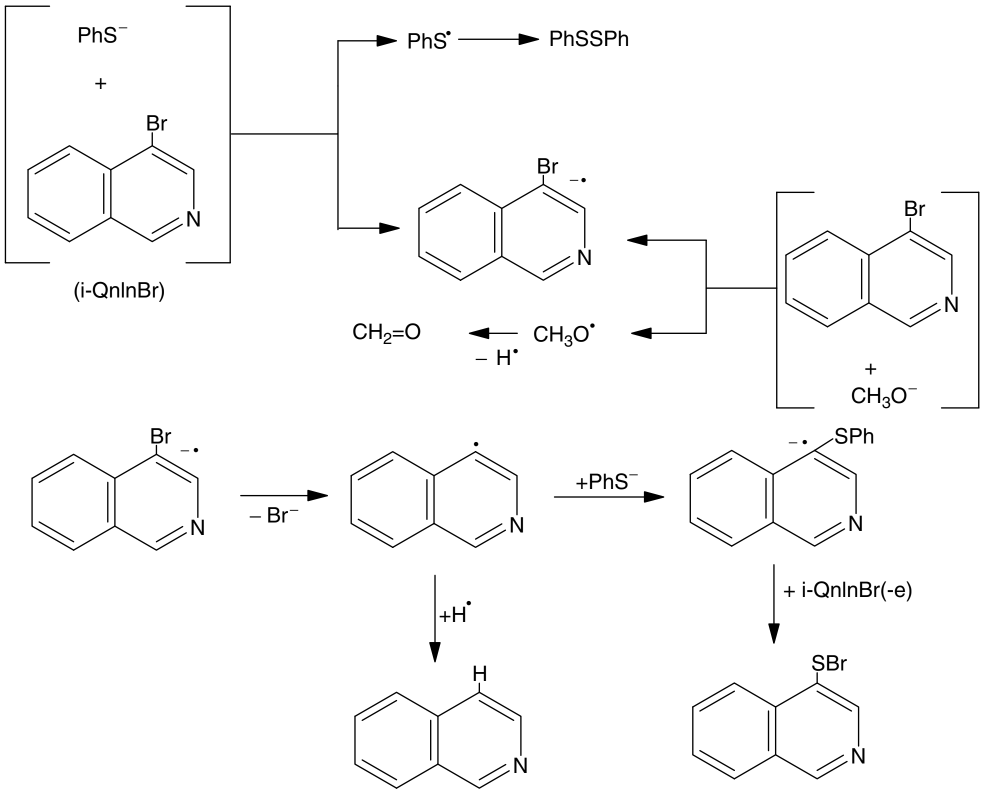
Some chemical additives can induce ion-radical formation and direct the reaction along the ion-radical route. The effect was discovered and studied in cases of nucleophilic substitutions of cumene derivatives (Kornblum 1975, 1982). Cumyl radicals are formed at the first step of substitution irrespective of whether a dissociative or homolytic cleavage takes place as a result of electron transfer to the cumene derivatives (Zheng et al. 1999).

As it turned out, the cumyl radical could be trapped not only by those nucleophilic ions, part of which were spent to generate the initial anion-radicals, but also with other anions. Hence, the products of substitution may also be formed with anions that either do not enter into a common reaction with the substrate or react with it slowly. In other words, a very small amount of a reactive nucleophile may induce the reaction.

Thus, sodium azide and α,*p*-dinitrocumene do not react unless subjected to the action of light (48 h control period). In contrast to sodium azide, the lithium salt of 2-nitropropane reacts with α,*p*-dinitrocumene in the dark for 3 h, giving the product of α-substitution in 87% yield. When α,*p*-dinitrocumene (1 mol) is treated with sodium azide (2 mol) in the presence of the lithium salt of 2-nitropropane (only 0.1 mol), the initial α,*p*-dinitrocumene quantitatively converts into *p*-nitrocumyl azide for 3 h. The product is extremely pure, and the reaction requires no UV irradiation (Kornblum et al. 1970) (Scheme 5.6).



SCHEME 5.6

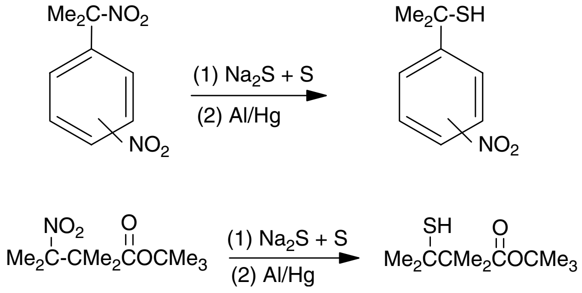


SCHEME 5.7

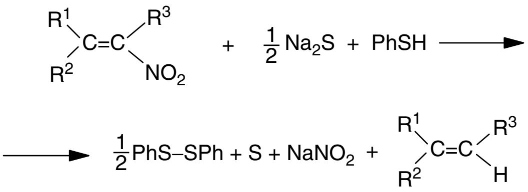
Typical one-electron donors, for example, sodium naphthalene, also entrained the reaction of *p*-nitrocumyl chloride with sodium nitrite (Kornblum et al. 1970).

Zoltewicz and Oestreich (1973) employed sodium methylate to accelerate the reaction between 4-bromo-iso-quinoline and sodium thiophenolate. In this case, the CH_3O^- ion acts as a competing electron donor with respect to the PhS^- ion. On electron transfer to the substrate, thiophenolate converts into the phenylthiyl radical and then to diphenyldisulfide. Diphenyldisulfide is inactive in further transformations. The methylate ions generate the anion-radicals of the substrate, thus preserving the greater part of the thiophenolate for use in substitution. The observed rate of thioarylation and the yield of 4-phenylthio-iso-quinoline increase in the presence of sodium methylate. Azobenzene inhibits the action of sodium methylate. Scheme 5.7 summarizes what has been mentioned.

It is important to note that sodium methylate initiates only the formation of 4-phenylthio-iso-quinoline; the product of the competing substitution, 4-methoxy-iso-quinoline, is produced only in traces. The methylate ion, however, converts a part of the iso-quinolyl σ-radicals into the unsubstituted iso-quinoline and produces formaldehyde.



SCHEME 5.8



SCHEME 5.9

Let us now consider the conversion of nitro compounds into mercaptanes. Nitro compounds were treated with a mixture of sodium sulfide with sulfur and after that, they were reduced with aluminum amalgam (Kornblum and Widmer 1978) (Scheme 5.8).

The first stage of the synthesis involves the interaction of a nitro compound with sodium sulfide. When used alone, sodium sulfide is only slightly effective: The reactions proceed slowly and the yields of mercaptanes are small. If elemental sulfur is added, the conversion accelerates markedly and the yield increases to 75–80%. The promoting effect of elemental sulfur can be easily explained by the radical-chain mechanism. The reaction starts with one-electron transfer from the nucleophile to the nitro compound; further conversions resemble other chain ion-radical substitutions.

$$S^{2-} + S \rightarrow {}^{-}S\text{-}S_n^{-}$$

$$R_3\text{-}NO_2 + {}^{-}S\text{-}S_n^{-} \rightarrow (R_3C\text{-}NO_2)^{-\bullet} + {}^{\bullet}S\text{-}S_n^{-}$$

$$(R_3C\text{-}NO_2)^{-\bullet} \rightarrow NO_2^{-} + R_3C^{\bullet}$$

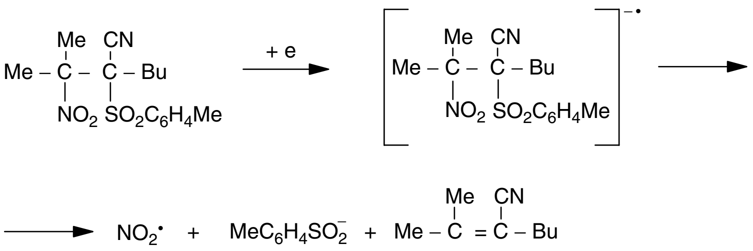
$$R_3C^{\bullet} + {}^{-}S\text{-}S_n^{-} \rightarrow R_3C\text{-}S^{\bullet}\text{-}S_n^{-}$$

$$R_3C\text{-}S^{\bullet}\text{-}S_n^{-} + R_3C\text{-}NO_2 \rightarrow (R_3C\text{-}NO_2)^{-\bullet} + R_3C\text{-}S\text{-}S_n^{-}$$

$$R_3C\text{-}S\text{-}S_n^{-} \xrightarrow{\text{Al/Hg}} R_3C\text{-}S^{-} + S_n^{-}$$

Obviously, the donor activity of the nucleophile, that is, the sulfide ion is enhanced as the negative charge is dispersed along the polysulfide ion produced from the sulfide on the addition of elemental sulfur. This increases the mobility of electrons and facilitates electron transfer. That is why this reaction can be initiated in such a simple way as the addition of elemental sulfur.

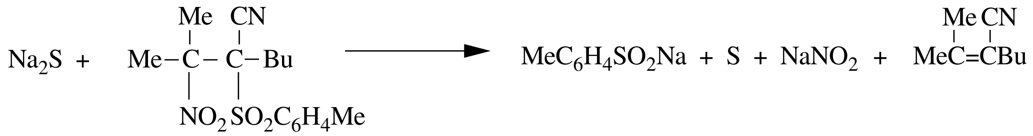
The chemical entrainment method was used by Ono et al. (1979) to eliminate the nitro group in nitroalkene derivatives. On simple mixing with thiophenol and sodium sulfide in DMF, nitro aryl olefins substitute hydrogen for the nitro group (Scheme 5.9).



SCHEME 5.10

The authors hold the opinion that the thiophenolyc moiety adds to the olefin bond and an electron adds to the nitro group. Hence, the anion-radical $[R^1R^2C(SPh)CH(R^3)NO_2]^{-\bullet}$ controls the reaction. The final product is formed as a result of the cleavage of the latter anion-radical with the expulsion of the nitrite ion and the phenylthiyl radical. The radical normally transforms into diphenyldisulfide. The yields of the denitrated olefines are high and reach 80–95%.

The production of olefines from β-nitrosulfones provides another type of effect of the chemical additives. The reaction is conducted in DMF without light irradiation using sodium sulfide as a reactant. The olefin forms in 97% yield (Ono et al. 1980, 1983).



This process is of interest because the reaction reveals an unexpected effect of such additives, which usually hinder anion-radical reactions. According to the authors, the considered reaction has the ion-radical mechanism (Scheme 5.10).

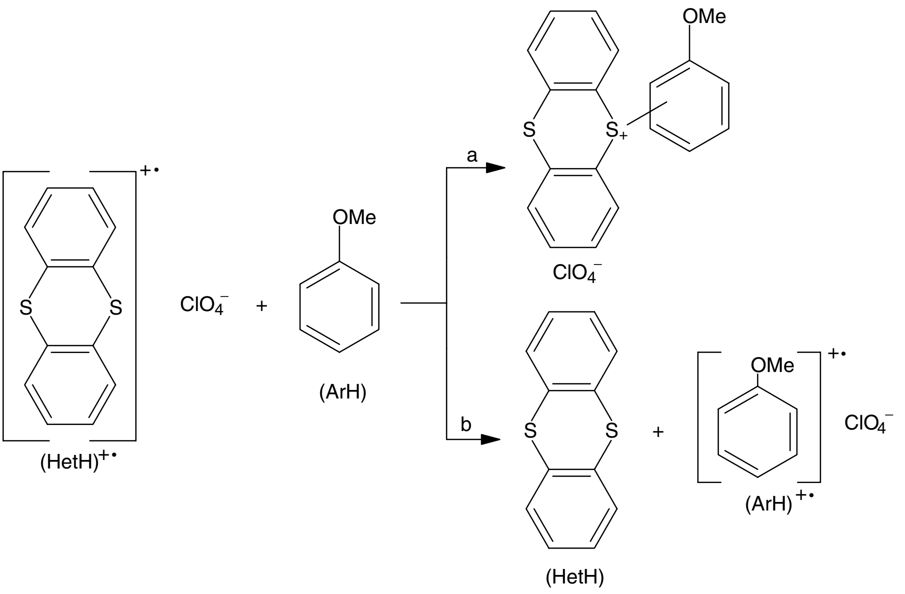
The authors attribute the olefin formation to elimination of the sufinate ion and nitrogen dioxide. Small amounts of di-*tert*-butylnitroxide (5 mol%) completely inhibit the production of olefin. This points to the chain free-radical nature of the process. Aromatic nitro compounds, which remove electrons from the anion-radical participating in the reaction, usually inhibit ion-radical conversions. In the reaction of Scheme 5.10, *m*- and *p*-dinitrobenzene (in amounts not exceeding 10 mol%) markedly accelerate the reaction. Three acceptor groups (NO_2, CN, and SO_2Ar) in the anion-radical seemingly keep an unpaired electron from being removed with the leaving group. Probably, on addition of aromatic nitro compounds in the reaction sphere, a donor–acceptor complex is formed with the substrate anion-radical. The unpaired electron shifts to a π acid (dinitrobenzene) in the framework of the complex. This increases electron mobility and catalyzes elimination of a leaving group taking the superfluous electron away.

Consequently, in ion-radical reactions, inhibitors may become promoters. This should also be taken into account when developing ways to stimulate reactions of an ion-radical nature.

The reactions discussed so far involved anion-radicals. Now let us discuss the conversions of the cation-radical type. One of these reactions is anisylation of the thiantrene cation-radical (Svanholm et al. 1975, Hammerich and Parker 1982) (Scheme 5.11).

The reaction in Scheme 5.11 gives the sulfonium salt (anion ClO_4^-) in a 90% yield (route a). One-electron reduction of the thianthrene cation-radical by anisole is the side reaction (route b). Route b leads to products with a 10% total yield. Addition of the dibenzodioxine cation-radical accelerates the reaction 200 times. The cation-radicals of thianthrene and dibenzodioxine are stable. Having been prepared separately, they are introduced into the reaction as perchlorate salts.

When the concentration of the thianthrene cation-radical drops from 10^{-3}–10^{-4} M to 10^{-5} M, the reaction results change: The sulfonium salt is not produced at all (route a becomes closed) and



SCHEME 5.11

one-electron transfer remains the sole process (route b). Kinetic studies (Svanholm et al. 1975) have established that the anisylation of the thianthrene cation-radical involves the following stages:

1. The formation of the thianthrene cation-radical complex with anisole, that is, $(HetH)^{+\bullet} + ArH \rightarrow (HetH\cdots ArH)^{+\bullet}$
2. The oxidation of the cation-radical complex into the dication, that is, $(HetH\cdots ArH)^{+\bullet} - e \rightarrow (HetH\cdots ArH)^{2+}$
3. Rapid deprotonation of the dicationic complex yielding the final product, sulfonium salt, that is, $(HetH\cdots ArH)^{2+} \rightarrow (HetH\text{-}Ar)^{+}$

The key stage of the process is the formation of the dicationic complex $(HetH\cdots ArH)^{2+}$. This stage determines the rate of the whole reaction. Therefore, the final result of the reaction should depend on the stationary concentration of this complex. From this, the following ways of regulating the process can be inferred:

To *increase* the stationary concentration of complex $(HetH\cdots ArH)^{2+}$, a stronger oxidizer, as compared to the cation-radical of thianthrene, should be introduced into the reaction. This is the cation-radical of dibenzodioxine. It increases the rate of the reaction by 2 orders.

To *decrease* the stationary concentration of complex $(HetH\cdots ArH)^{2+}$, it will suffice to lower the concentration of the oxidizer, that is, substrate $(HetH)^{+\bullet}$. This also decreases the equilibrium concentration of the cation-radical complex $(HetH\cdots ArH)^{+\bullet}$. The rate of anisylation—the main process—drops sharply. The side process, one-electron transfer from anisole to the cation-radical of thianthrene, also decelerates, but not so markedly. So this side process (route b on Scheme 5.11) remains the only one.

Cycloaddition of dimethylbutene (DMB) to the thianthrene cation-radical $[(HetH)^{+\bullet}]$ also includes the stage of complexation and oxidation, but in this case the same $(HetH)^{+\bullet}$ is capable of being an additional oxidant (Zhao et al. 2006):

$$(HetH)^{+\bullet} + DMB \rightarrow (HetH\cdots DMB)^{+\bullet}$$

$$(HetH\cdots DMB)^{+\bullet} - e \rightarrow (HetH\cdots DMB)^{2+}$$

The same way was used by Yoon and Kim (2005) for the preparation of 5-(*p*-methoxyphenyl)thian threnium ion incorporated in a calyx[4]arene. Namely, the ratio of starting materials, methoxycalixarene to the thianthrene cation-radical perchorate, was 1:10. The product of such "*S*-anisylation" of thianthrene was further transformed into a calixarene bearing an additional *o*-phenylene thiomacrocycle. This macrocylization is beyond the scope of this book; the original paper by Yoon and Kim (2005) could be recommended for those who interested in. It is worth noting only one practical importance of the calixarene-phenylene thiomacrocycle here: It selectively extracts silver(1+) by both calixarene and thiomacrocycle. Each molecule of this combined complexon takes up two silver cations, so that extractability achieves 165%.

Shono et al. (1979) recommend the use of thioanisole as a catalyst that allows lowering the electrode potential in the oxidation of the secondary alcohols into ketones. The cation-radical of thioanisole is generated at a potential of up to +1.5 V in acetonitrile containing pyridine (Py) and a secondary alcohol. (The background electrolyte was tetraethylammonium *p*-toluene sulfonate.) Thioanisole is recovered and, therefore, a ratio of $R^1(R^2)CHOH{:}PhSMe = 1{:}0.2$ is sufficient. The yield of ketones depends on the nature of the alcohol and varies from 70 to 100%.

$$\mathrm{PhSMe} \xrightarrow[-e]{} (\mathrm{PhSMe})^{+\bullet}$$

$$\mathrm{R^1(R^2)CHOH} + (\mathrm{PhSMe})^{+\bullet} \longrightarrow \mathrm{R^1(R^2)CHO}-\overset{+}{\mathrm{S}}(\mathrm{Me})\mathrm{Ph} + \mathrm{H^+}$$

$$\mathrm{Py} + \mathrm{H^+} \longrightarrow \mathrm{PyH^+}$$

$$\mathrm{R^1(R^2)CH\text{-}O\text{-}}\overset{+}{\mathrm{S}}(\mathrm{Me})\mathrm{Ph} \longrightarrow \mathrm{PhSMe} + \mathrm{R^1(R^2)C{=}O}$$

Let us now turn to the role that oxygen plays in ion-radical conversions. As a component of air, oxygen is typically an active part of the medium in which chemical conversions mainly proceed.

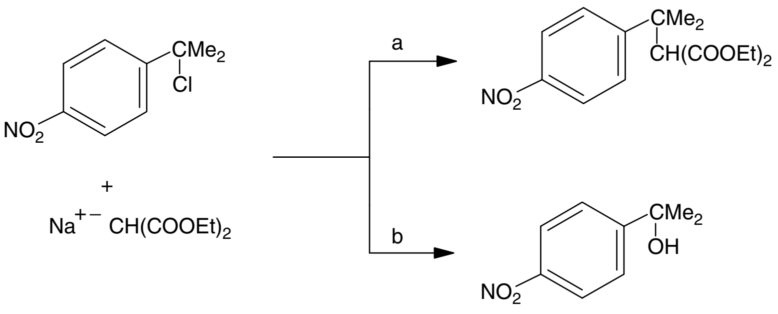
Cation-radicals are often unstable and dissociate. If the dissociation is a reversible process, oxygen promotes it, because oxygen reacts with fragment ions and radicals, which are produced in the decomposition. In other words, oxygen shifts the equilibrium to the right. Therefore, scientists prefer to conduct reactions with cation-radical participation in an inert atmosphere, although oxygen (air) is, strictly speaking, inert with respect to primary cation-radicals. Exceptions to this are only those reactions (e.g., biological ones) where oxygen is required to obtain cation-radicals from neutral molecules.

For anion-radicals, air (i.e., oxygen, carbon dioxide, and water [moisture]), on the whole, is an active component of the medium and so it should be removed before conducting reactions. Understandably, air inhibits anion-radical reactions: The anion-radicals primarily formed are consumed at the expense of oxidation, carboxylation, and protonation. Certainly, oxidation can take place only if the acceptor organic molecule possesses a lower affinity for an electron than oxygen does or if one-electron oxidation of the anion-radical by oxygen proceeds more rapidly than the anion-radical decomposition into a radical and an anion ($RX^{-\bullet} \rightarrow R^{\bullet} + X^{-}$).

If the oxidation is slower than the decomposition, oxygen may affect the nature of reaction products. Thus, treating *p*-nitrocumyl chloride with sodium malonate ester in a flow of pure dry nitrogen yields a product of *C*-alkylation (route a in Scheme 5.12); the yield is 90%. Oxygen completely inhibits the *C*-alkylation, and the reaction gives *p*-nitrocumyl alcohol in the same yield (route b in Scheme 5.12) (Kornblum et al. 1968).

When the malonate is absent, oxygen is incapable of converting *p*-nitrocumyl chloride into alcohol (Kornblum et al. 1968).

In the presence of oxygen, the reaction in Scheme 5.12 develops in two directions with different rates. The reaction first produces anion-radicals of *p*-nitrocumyl chloride (the sources of electrons



SCHEME 5.12

are the malonate anions), and then chloride ions cleave from these anion-radicals. Nitrocumyl radicals accumulate at a faster rate than the initial anion-radicals perish under the effect of oxygen. Therefore, oxygen may trap only cumyl radicals and give cumyl peroxide radicals, which convert into the hydroperoxide when abstracting hydrogen from the solvent. The hydroperoxide decomposes and forms cumyl alcohol. Because the yield of the alcohol reaches 90%, the conclusion follows that the conversion is highly selective. It follows the sequence:

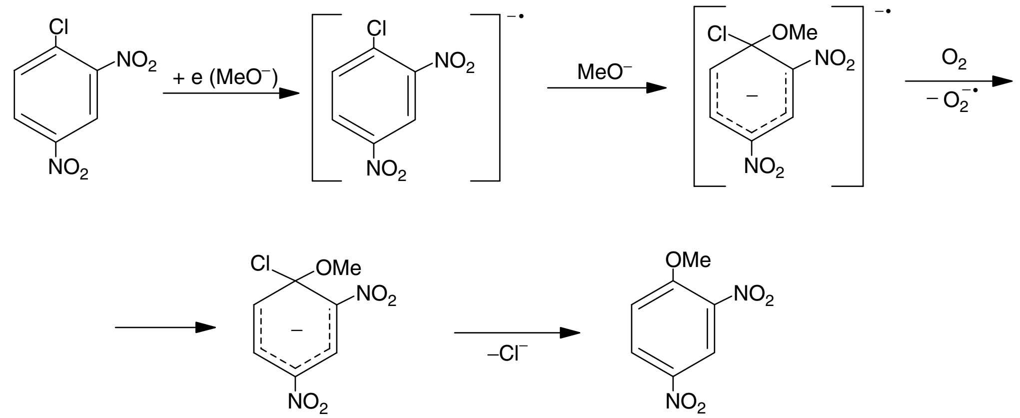
$$4\text{-}O_2NC_6H_4C(Me)_2Cl \xrightarrow{NaCH(COOEt)_2} \left[4\text{-}O_2NC_6H_4C(Me)_2Cl\right]^{-\bullet} \longrightarrow$$

$$\xrightarrow[-Cl^-]{} 4\text{-}O_2NC_6H_4\dot{C}Me_2 \xrightarrow{O_2} 4\text{-}O_2NC_6H_4CMe_2(OO^\bullet) \longrightarrow$$

$$\longrightarrow 4\text{-}O_2NC_6H_4CMe_2(OOH) \xrightarrow[-O]{} 4\text{-}O_2NC_6H_4CMe_2(OH)$$

Then the case is possible when the acceptor ability of oxygen is lower than that of the substrate, but greater than that of the charged (intermediary or final) products of anion-radical conversions. The superoxide ion is produced in the finishing stages of the process and acts as an electron carrier with respect to the substrate, thus branching the chain process. In other words, oxygen promotes rather than inhibits these reactions. This case is especially important for the practice of organic synthesis. As reported (Omelechko et al. 1982), the reaction between 1-nitroanthraquinone and sodium methylate in the mixture of DMSO with methanol accelerates when conducted in air and not under argon. Being obtained by a cathode reaction in DMSO under the controlled (inert) atmosphere, anion-radicals of 1-nitroanthraquinone do not change on the addition of MeOH or MeONa. When air gains access to the system, the anion-radicals are consumed completely and produce 1-methoxyanthraquinone (the main product) and 1-hydroxyanthraquinone (the admixture). Oxygen, therefore, promotes methoxylation via the anion-radical mechanism. An earlier study revealed that methoxylation of 2,4-dinitrochlorobenzene accelerates by an order of magnitude when conducted in air rather than in nitrogen and the mechanistic Scheme 5.13 was proposed (Blumenfel'd et al. 1970).

As seen from Scheme 5.13, not the initial substrate, but rather its anion-radical undergoes methoxylation. This produces the anion-radical of the σ complex, which is oxidized by oxygen into the conventional anionic σ complex carrying no unpaired electron. This stage generates the superoxide ion, which later competes advantageously with the methoxide ion for the starting 2,4-dinitrochlorobenzene to reduce it into the anion-radical.



SCHEME 5.13

The main point, with respect to the catalytic effect of oxygen, is the ability of the superoxide ion to transfer electrons to strongly accepting molecules of the substrate. This was confirmed by electrochemical generation of the superoxide ion: In DMF, *o*- or *p*-nitrochlorobenzene and *o*-nitrobromobenzene react with $O_2^{-\bullet}$ giving *o*- and *p*-nitrophenol (Sagae et al. 1980). Frimer and Rosenthal (1976) treated 2,4-dinitrobromobenzene with $K^{18}O_2$ in the presence of dicyclohexane-18-crown-6-ether (the solvent was benzene saturated with $^{16}O_2$) and obtained 2,4-dinitrophenol carrying practically no ^{18}O. According to mass-spectrometric data (Frimer and Rosenthal 1976), the content of the label in phenol was below 10%. Hence, superoxide ion $^{18}O_2^{-\bullet}$ only transfers an electron to the substrate, and phenol is produced as a result of the reaction between the anion-radical of 2,4-dinitrobromobenzene or the 2,4-dinitrophenyl radical and oxygen-$^{16}O_2$.

It should be emphasized that reactions conducted in traditional ways under inert gaseous atmosphere may sometimes fail. Oxygen accelerates the reactions involving strong acceptor substrates. This is similar to a promoting effect of active organic oxidizers of the dinitrobenzene type. The first example of such catalytic reactions was described almost half a century ago (Russell 1954). A carbanion (R^-) reacts with O_2 according to the mechanism of catalysis with a one-electron transfer:

$$R^- + O_2 \rightarrow R^\bullet + O_2^{-\bullet}$$

$$R^\bullet + O_2 \rightarrow ROO^\bullet$$

$$ROO^\bullet + R^- \rightarrow ROO^- + R^\bullet$$

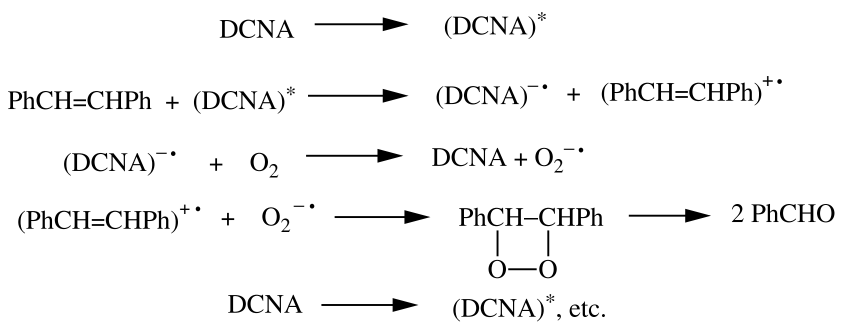
$$ROO^- \rightarrow RO^- + O$$

$$O + O \rightarrow O_2$$

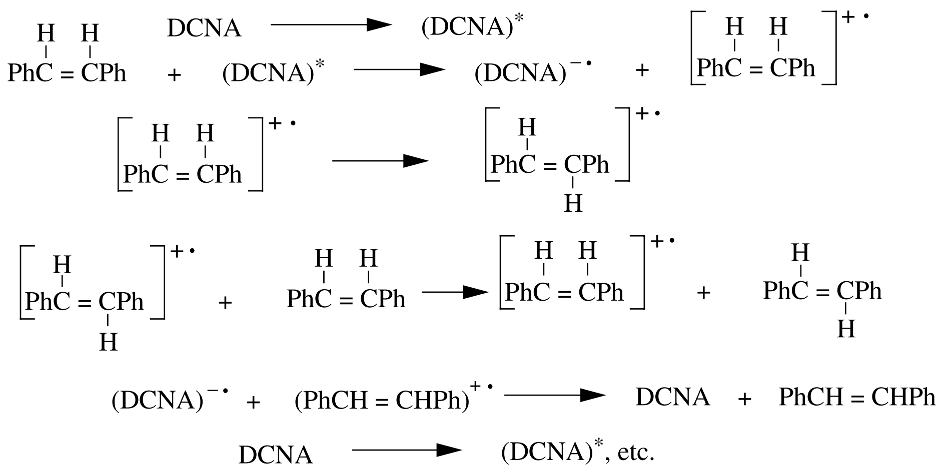
$$R^\bullet + O_2 \rightarrow ROO^\bullet, \text{etc.}$$

Electron-transfer catalytic cycles with oxygen were also discovered in photochemical reactions with participation of an excited sensibilizer (9,10-dicyanoanthracene [DCNA]) and stilbene. The sensitizer assists an electron transfer from the substrate to oxygen. Oxygen transforms into the superoxide ion. Stilbene turns into benzaldehyde. In the absence of the sensitizer, this reaction does not take place even on photoirradiation (when oxygen exists in the first singlet state). In the singlet state,

oxygen acquires enhanced oxidative ability, but only to a limited degree. Juillard and Chanon (1983) describe the events by the following transitions:



In the absence of oxygen, photoirradiation of stilbene with the same sensitizer (DCNA) provokes cis → trans isomerization of the olefine. The reaction is initiated with a 365 nm light and proceeds at 25°C (Lewis et al. 1985):



This reaction gives us an opportunity to consider the roles of the salt additive, the solvent polarity, the stilbene concentration, the temperature level, and the intensity of potoirradiation. The reaction is facilitated by the replacement of a nonpolar solvent (benzene) by a polar one (acetonitrile), a rise in reaction temperature, an increase in the stilbene concentration, a decrease in the irradiation intensity, or the addition of alkali metal salts. All of these factors intensifying the process are directly related to the mechanism just described. It is substantial enough to analyze the effects of these factors on the efficiency of the photoreaction.

An increase in the *cis*-stilbene concentration favors the chain propagation and decreases the probability of termination when the DCNA anion-radicals react with the stilbene cation-radicals. A decrease in the irradiation intensity has a similar effect: The chain propagation is the first-order process, whereas termination of the chains is the second-order process. A temperature rise accelerates the accumulation of the stilbene cation-radicals. In this system, the free energy of electron transfer is $-53 \div -44$ kJ · mol^{-1} (the cation-radical generation is in fact an endothermal process). If a polar solvent is substituted for a nonpolar one, the conversion of the *cis*-stilbene cation-radical into the *trans*-stilbene cation-radical deepens. Polar solvents break ion pairs, releasing free ion-radicals. The *cis*-stilbene cation-radicals isomerize more easily on being released. The stilbene cation-radical not shielded with a counterion has a more positive charge, and therefore, becomes stabilized in the

more polar solvent. In other words, isomerization is less effective when (*cis*-stilbene)$^{+•}$ forms an ion pair with (DCNA)$^{-•}$. When $NaClO_4$ (alkali metal salt) is added, (DCNA)$^{-•}$ becomes bonded in another (more compact and therefore more stable) ion pair, namely (DCNA)$^{-•}$Na^{+}. As a result, the cation-radical of *cis*-stilbene is liberated from the formerly existing ion pair with (DCNA)$^{-•}$. In addition, chain termination caused by interaction of the stilbene cation-radicals with the DCNA anion-radicals (the back electron transfer) becomes less probable because the cation-radicals and the anion-radicals are not so close to each other as in a united ion-radical pair (IRP).

This example shows the important role of the solvent's nature and the salt's addition in ion-radical transformations. These two significant factors are examined in the following two sections.

5.4 SOLVENT EFFECTS

Ion-radical organic reactions in solutions are among the most important reactions in chemistry and biology. A particularly significant question in chemical reaction dynamics in solutions is the influence of the solvent on the direction and the rate of the reaction. Medium effects on electron-transfer reactions (which lead to the ion-radical formation) are usually classified as static and dynamic interactions between the solvent and reacting solutes. Static effects refer to the stabilization of reactants, transition states, and products, that is, how the solvent affects the free energies of these species and the activation energy of the reaction. This interpretation of solvent effects on all kinds of chemical reactions is well established. There is an extensive body of reviews and monographs on the topic. A recent development is the investigation of the influence of solvent dynamics on the reaction rates. Articles by Heitele (1993), Drago and Ferris (1995), and Leite (1999) have described these modern developments in the theory and experimental study of electron-transfer processes especially. The transfer of an electron is triggered by a fluctuation of the dielectric polarization in the surrounding solvent. Formation of ion-radicals, which are a more polar component of the solution than the starting neutral molecules, can lead to nonspecific (nonbonding) solvation. The term "specific solvation" is meant to describe some selectivity in interaction between a solvent and a solute skeleton fragment, in distinction from a general (bulk) dielectric effect.

5.4.1 Static Effects

The fewer factors that lower ion-radical stability, the more easily ion-radical organic reactions proceed. Because ion-radicals are charged species with unpaired electrons, solvents for the ion-radical reactions have to be polar too, incapable of expelling cationic or anionic groups that the ion-radical bears as well as chipping off radicals from it (especially to abstract the hydrogen atom). Static solvent effects can be subdivided on general and specific ones.

5.4.1.1 General Solvation

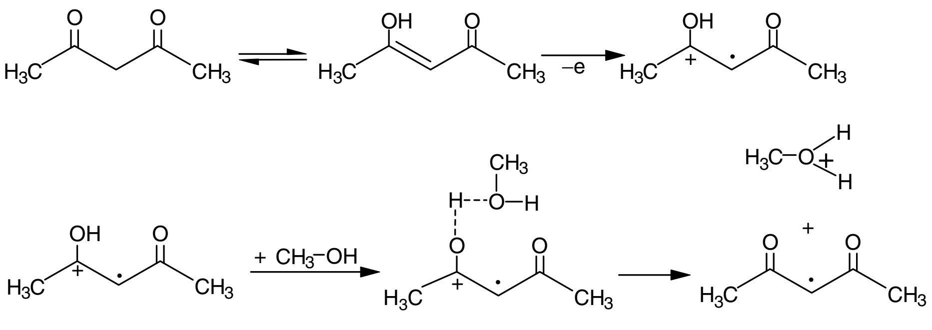
Photoinduced electron transfer from 4-chlorophenylthiolate to 2-nitro-2-thiocyanato propane leads to the formation of the following IRP (Al-Khalil and Bowman 1984):

$$4\text{-ClC}_6\text{H}_4\text{S}^- + \text{Me}_2\text{C(NO}_2\text{)SCN} \rightarrow \{4\text{-ClC}_6\text{H}_4\text{S}^{•}, [\text{Me}_2\text{C(NO}_2\text{)SCN}]^{-•}\}\ (\text{IRP})$$

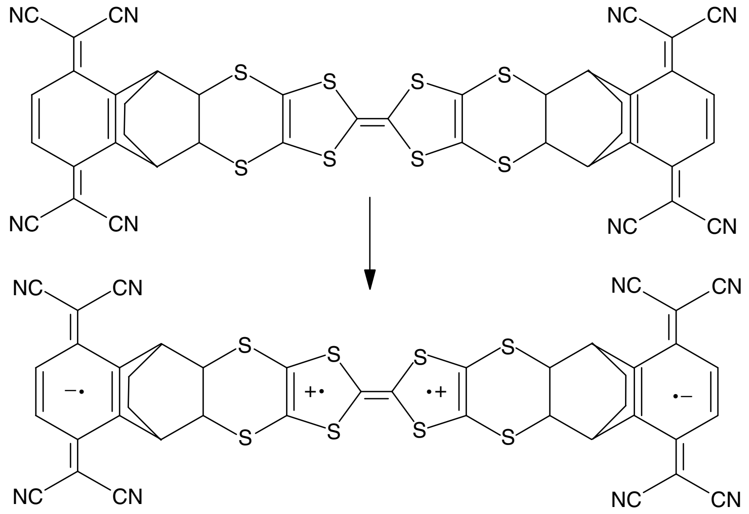
The final destiny of IRP depends on the nature of the solvent. In DMSO, the main process is an inner-cage recombination (route a), a minor process consists of IRP disintegration after its diffusion into volume (route b):

1. IRP $\rightarrow$ 4-$ClC_6H_4SC(NO_2)Me_2$ + ^{-}SCN
2. IRP $\rightarrow$ 4-$ClC_6H_4SSC_6H_4Cl$-4′ + ^{-}SCN + $Me_2C{=}NOO^-$

Both routes, a and b, are nonchain processes because the yields of the final products (54 and 35%, respectively) do not change on addition of *p*-dinitrobenzene and *tert*-butylnitrone as well as in the



SCHEME 5.14



SCHEME 5.15

presence of oxygen. Substitution of MeOH for DMSO as a solvent suppresses route a entirely. As suggested (Al-Khalil and Bowman 1984), the presence of a proton in the methanol solvent cage stabilizes the nitro thiocyanate anion-radical $[Me_2C(NO_2)SCN]^{-\bullet}$ by means of hydrogen bonding. Such stabilization prevents inner-cage recombination and contributes to diffusion of the electron-transfer products into the solution volume.

Hydrogen bonding between an ion-radical and solvent may also enhance the ion-radical reactivity. Thus, the formation of hydrogen bond between methanol and the β-diketone cation-radical accelerates its deprotonation according to Scheme 5.14 (Jiao et al. 2007).

Stabilization by a solvent can often determine the very initial step consists of ion-radical generation. Hence, alkali metal hydroxides are highly stabilized in water and in aqueous organic solvents, and therefore, their reactivities in simple one-electron processes are either very low or practically nonexistent. Alkali-metal hydroxides are at least somewhat soluble, particularly in the presence of water traces, in polar solvents (DMSO, HMPA, THF). In these solvents, the HO^- solvation is drastically diminished (Popovich and Tomkins 1981). As a result, reactions of one-electron transfer from the hydroxy anion to the substrate take place (Ballester and Pascual 1991).

Potassium hydroxide when merely dissolved in methanol is not effective in the one-electron reduction of 9-diazofluorene and fluoren-9-ylides. Addition of DMSO to the system makes a drastic change, with the highest efficiency in pure DMSO (Handoo and Kaul 1992, Handoo et al. 1983).

It should also be mentioned that cases are possible when polarity of the solvent allows transforming charge-transfer intramolecular complexes into molecules containing the cation- and anion-radical

moieties, that is, into the states with full separation of the positive and negative charges. Such phenomenon was demonstrated by Tsiperman et al. (2005) by means of changing nonpolar dichloromethane or toluene to strongly polar DMF as a solvent. Scheme 5.15 depicts this transition from the inner CTC (containing partial charges δ+ within the tetrathiafulvalene moiety and δ− within the TCNQ moieties) into the inner dianion-dication-tetraradical.

Nelsen et al. (2007) have revealed one more aspect of solvent control over charge localization. Solvents with marked electron-donor properties contribute to charge localization in cation-radicals, whereas anion-radicals experience the same changes in better electron-accepting solvents. Thus, naked (non-ion-paired) anion-radicals of 4,4′-dinitrostilbene and 4,4′-dinitrotolane show the spectra of delocalized species in HMPA and THF, but essentially spectra of localized species in DMF, DMSO, and MeCN.

5.4.1.2 Selective Solvation and Solute-Solvent Binding

With increasing solvent polarity, the very spin-charge distribution can be changed in ion-radicals. A typical example is the cation-radical of 9,10-bis{4-[*N*,*N*-di(4-methoxyphenyl)amino]phenylethenyl} anthracene (Noell et al. 2007). Weak polar media stabilize the form with the charge being mainly localized at the anthracene bridge and at attached alkyne groups. Strong polar media (acetonitrile) stabilize the form with the "normal" (terminal) charge localization in the vicinity of the amino function. In this case, oscillation of the charge takes place between the two 4-[*N*,*N*-di(4-methoxyphenyl)amino] terminal functions through the bridge-conjugated system. Analogous phenomena have been described earlier by Nelsen et al. (1998), El-Ghayoury et al. (2000), Kilsa et al. (2001), Holzapfel et al. (2002), Fraysse et al. (2003), Karafiloglou and Launay (2003), and Lambert et al. (2004). Solvation of this bridged cation-radical is infirm in the weak polar solvent. The strong polar solvent is able to solvate the aminiumyl moiety selectively. This results in fixation of the reorganized electron structure.

Besides solvation, a solvent can also participate in entrainment of ion-radical transformations. The reaction between tertiary aliphatic nitro compounds and the sodium derivative of nitromethane, $NaCH_2NO_2$, is an example (Kornblum and Erickson 1981). To prepare $NaCH_2NO_2$, nitromethane is treated with sodium hydride. Then a tertiary aliphatic nitro compound is introduced into the solution formed. Several organic solvents were probed and $CH_3SO_2CH_3$ (DMSO) turned out to be the most effective. Kornblum and Erickson (1981) attributed this result to the formation of small amounts of $NaCH_2SOCH_3$ (sodium dimsyl) that was produced from DMSO as a result of its reaction with sodium hydride. Sodium dimsyl acts as a powerful one-electron reducer that induces the following chain anion-radical process:

$$Me_2RCNO_2 + NaCH_2NO_2 \rightarrow Me_2RCH_2NO_2 \rightarrow Me_2RCHO$$

$$Me_2RCNO_2 + NaCH_2SOCH_3 \rightarrow (Me_2RCNO_2)^{-\bullet}Na^+ + CH_3SOCH_2^{\bullet}$$

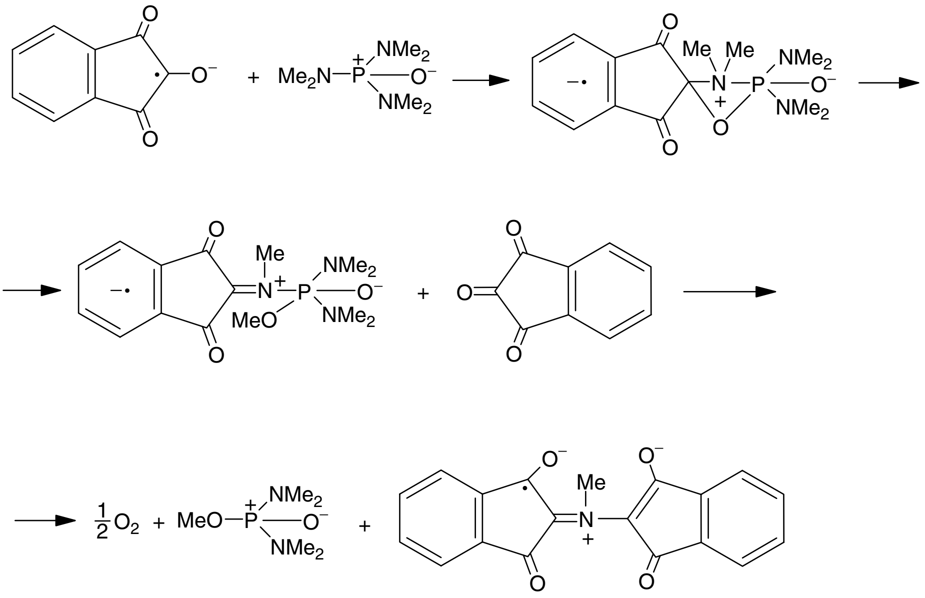
$$(Me_2RCNO_2)^{-\bullet}Na^+ \rightarrow NaNO_2 + Me_2RC^{\bullet}$$

$$Me_2RC^{\bullet} + NaCH_2NO_2 \rightarrow (Me_2RCNO_2)^{-\bullet}Na^+, \text{ etc.}$$

$$CH_3SOCH_2^{\bullet} + H^{\bullet} \rightarrow CH_3SOCH_3$$

Another principal example concerns the solute-solvent bonding. Stevenson's group studied transformation of indantrione in HMPA. HMPA exhibits itself as a solvent, a one-electron donor, and a nucleophilic agent during dissolution of indantrione. Dissolution of indantrione in dry HMPA under high vacuum yields a paramagnetic solution. According to the ESR spectrum, the indantrione anion-radical (semitrione) is formed. After a period of 3–4 h, a new radical was fixed by ESR method. Its structure is depicted at the very end in Scheme 5.16 (Schertz et al. 2001).

The active role of the solvent may appear as hydrogen bonding involving participants of ion-radical organic reactions. From this point of consideration, fluorinated alcohols are by far the most illustrative solvents. Eberson et al. (1996) put into operation 1,1,1,3,3,3-hexafluoropropan-2-ol (HFP). This solvent differs in a rare combination of low nucleophilicity, high hydrogen-bonding donor strength, low hydrogen-bonding acceptor strength, high polarity, and high ionizing power. It allows the use



SCHEME 5.16

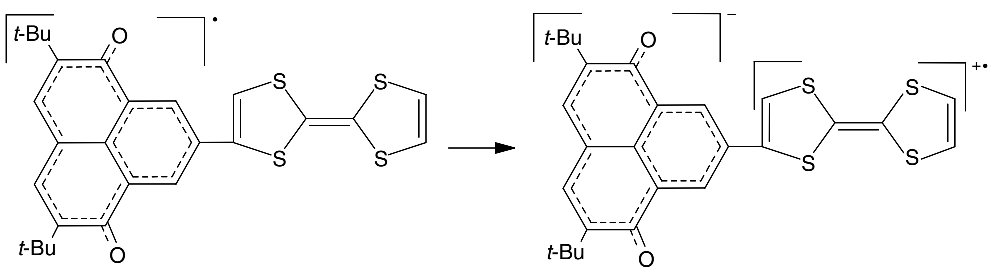
of mild conditions for the generation of cation-radicals from chemically sensitive compounds and avoids the need of cooling or the use of flow systems. In comparison to trifluoroacetic acid (a common solvent for generation of cation-radicals, see Chapter 2), HFP is 10^9 times less acidic, although it has the proton-donor hydroxyl group. Therefore, it is also convenient for generating cation-radicals that are acid sensitive. This solvent is very active at solvation of anions, whereas cations it solvates poorly. Being a weak hydrogen-bond acceptor, HFP is uniquely strong as a hydrogen-bond donor.

Galli's group reveals a specific role of HFP in stabilization of cation-radicals, comparing iodination of durene or mesitylene by means of iodine chloride in various organic solvents. In common solvents, the polar (conventional) mechanism is held. In HFP, the ion-radical mechanism of iodination takes over (Fabbrini et al. 2001). The specific role of HFP in one-electron reversible oxidation of *N,N,N′,N′*-tetramethyl-1,4-phenylenediamine (TMPDA) is also worth noting. In Chapter 1, it has already been shown that TMPDA cation-radical is a perfectly delocalized system. Potential of its formation from TMPDA slightly depends on the nature of common organic solvents. However, in HFP, such potential becomes markedly less positive. HFP stabilizes the cation-radical formed and this is reflected in the facilitation of the electrochemical oxidation. The stabilization is attributed to extremely high hydrogen-bond donor ability of HFP (Svith et al. 2004). The scope and limitations of HPF applicability as a solvent for ESR spectral observation of cation-radicals as well as for anode electrochemistry are detailed by Eberson et al. (1995, 1996) (see also Tabakovic et al. 1996, Barbosa et al. 1998).

Trifluoroethanol (TFE, CF_3CH_2OH) also demonstrates high H-bond activity. The dyad system in which a radical and electron-donor parts are linked directly undergoes intramolecular electron transfer on substitution of TFE for toluene as a solvent. The transition was interpreted as a marked effect of hydrogen bonding (or reversible protonation) of the anionic R–O$^-$ structure with TFE (Nishida et al. 2005). Scheme 5.17 depicts this transition.

Workentin et al. (1994) described another interesting solvent effect on the competition between electron transfer and the addition reaction between organic cation-radicals and azides. TFE and AN were compared as solvents. In TFE, the cation-radicals of 4-methoxystyrene (R^1=R^2=H), β-methyl-4-methoxystyrene (R^1=Me, R^2=H), or β,β-dimethyl-4-methoxystyrene (R^1=R^2=Me) react with the azide ion according to the following equation:

$$(CH_3OC_6H_4CH{=}CR^1R^2)^{+\bullet} + N_3^- \rightarrow CH_3OC_6H_4CH^\bullet C(N_3)R^1R^2 + N_3^\bullet$$



SCHEME 5.17

Rate constants ($k \times 10^{-9}$ M^{-1} s^{-1}) were determined to be 7.0, 3.5, and 1.0 for the enumerated substrates, respectively. This change in kinetics coincides with the increase in steric hindrance at the β-carbon. Nevertheless, in AN, the rate constants were found to be equal for all the three styrenes (~3 × 10^9 M^{-1} s^{-1}). In AN, the reaction consists of one-electron transfer from the azide ion to a cation-radical. As a result, a neutral styrene and the azidyl radical are formed. The azidyl radical reacts with excess of the azide ion, and the addition reaction does not take place in AN:

$$(CH_3OC_6H_4CH{=}CR^1R^2)^{+\bullet} + N_3^- \rightarrow CH_3OC_6H_4CH{=}CR^1R^2 + N_3^\bullet$$

$$N_3^\bullet + N_3^- \rightarrow N_6^{-\bullet}$$

The change in mechanism from the addition of TFE to the electron transfer in AN is defined by the relative oxidation potentials of the styrenes and of the azide ion in these two solvents. For example, in AN, the oxidation potential of the azide ion is approximately 0.6 eV lower than that of the styrenes, indicating that electron transfer should occur at the diffusion-controlled rate as observed. The oxidation potentials of styrenes in TFE do not differ substantially from those in AN. However, the oxidation potential of the azide anion increases drastically in TFE, presumably due to stabilization of the anion by hydrogen bonding. The shift in oxidation potential means that electron transfer is not sufficiently exergonic to occur at a diffusion-controlled rate, allowing addition to compete effectively with electron transfer. The results demonstrate, on one hand, the importance of the hydrogen-bonding activity of a solvent and, on the other hand, the importance of redox properties (which reflect relative solvation energies) in determining the selectivity of ion-radical organic reactions.

One additional example involves alkylation of the lithium salt of the anthracene anion-radical by 2-octyl fluoride (Herbert et al. 1985). The akylation does not occur in DMF (which strongly solvates Li^+), whereas it is facilitated and leads to the quantitative yield in diethyl ether. Diethyl ether is much less active at solvation of the lithium cation. That makes >CH–F···Li^+ coordination possible and assists the formation of octylanthracene.

It is worth mentioning that there are some solvents that combine good solvency power with coordinating properties. The most salient example is 1,2-dimethoxyethane as a solvent in the reduction of organic acceptors by alkali metals. The acceptors transform into anion-radicals, and alkali metals into their cations. These cations are bound in chelates with 1,2-dimethoxyethane, and the one-electron reduction of the acceptors becomes more energy advantageous.

Another point of such coordination activity is the specific interaction of the solvents containing heteroatoms with cation-radicals having a suspended unpaired electron (cf. Chapter 3). A pertinent example in this context is the interaction between the dialkylsulfide cation-radicals and the oxygen belonging to the water molecule. Such interaction enhances stability of the "coordinated" cation-radical:

$$R_2S^{+\bullet} + H_2O \rightarrow (R_2S\therefore OH_2)^+$$

Of course, the strength of the intermolecular three-electron bond depicted is lower than that of the intramolecular three-electron bond (see Section 3.2.3). Interestingly, no dimer complex

$[(tert\text{-Bu})_2S{\therefore}S(tert\text{-Bu})_2]^+$ was formed. The strength of S∴S bond in this dimer is lesser than the strength of S∴O bond in the $[(tert\text{-Bu})_2S{\therefore}OH_2]^+$ complex (Asmus 1990).

Certainly, selective interaction is possible between a solvent and an ion-radical. The qiunone ion-radicals are examples. *Cation*-radicals of 1,4-benzoquinone alkoxy derivatives form very stable O–D bonds being frozen in the $D_2O–D_2SO_4$ solvent mixture (Spoyalov et al. 1992). The 1,4-benzoquinone *anion*-radical also forms stable hydrogen bonds with alcohols as solvents. Methanol-, ethanol-, and 2-propanol-OD were examined. Steric screening of the alcohol hydroxyl obviously plays no important role in hydrogen bonding with the 1,4-benzoquinone anion-radical. On formation of the anion-radical, the hydrogen bond gets shorter by about 0.025 nm as compared to the same bonds with the neutral 1,4-benzoquinone (Sinnecker et al. 2004). The phenomenon is close to redox-enhanced hydrogen bonding and stabilization of the ubiquinone anion-radical through complexation with thiourea (Greaves et al. 1999). Hydrogen bonding was established between an anion-radical of 1,4-bis(alkylether)-9,10-anthraquinone and the liquid ammonia solvent. In THF, this anion-radical undergoes conformational transition, whereas in NH_3 (liquid), the hydrogen bonding conserves the initial anion-radical structure (Kim and Stevenson 1999). Generation of hydroxide and the protonated quinone dianion during electron transfer to 3,5-di(*tert*-butyl)-1,2-benzoquinone can also be explained by the coordination of water with the quinone anion-radical (Lehman and Evans 2001).

It should also be mentioned that there are some cases when the cation-selective solvation promotes greater π-electron delocalization in the remaining "free" anion-radicals (see Section 3.2.5). Staley et al. (1999) and Staley and Kehlbeck (2001) studied the phenomenon for organic dianions too. Such a solvent effect leads to changes in reactivity of these species.

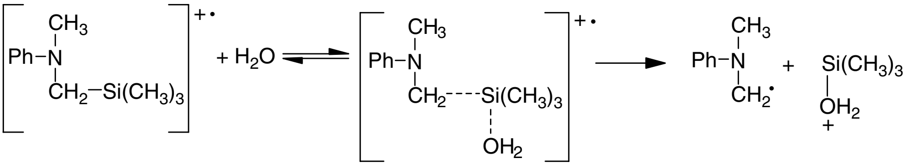
Hydrogen bonding can facilitate the transition of conventional ion-radicals into their distonic forms. The distonic forms have been discussed in Section 3.2.4. It is sufficient to mark here the corresponding transformation of the pyridine cation-radical in the presence of water (Ibrahim et al. 2007).

$$[C_5H_5N]^{+\bullet} + H_2O \rightarrow {}^{\bullet}C_5H_4NH^{+}\cdots H\text{–}OH$$

This kind of hydrogen bonding decreases the barrier of $C_5H_5N]^{+\bullet} \rightarrow {}^{\bullet}C_5H_4NH^+$ transition and makes the overall process more exothermic, that is, more energetically favorable.

Because selective solvation affects a specific group in an ion-radical, steric availability of this group plays an important role. Thus, $(PhSAlk)^{+\bullet}$ are mainly sulfur-centered cation-radicals, according to the analysis of their ESR spectra (Alberti et al. 1984) and B3LYP calculations (Baciocchi and Gerini 2004). The solvation of the positive charge on sulfur is very sensitive to the bulkiness of the S-bonded alkyl group: The oxidation potentials for PhSR in acetonitrile increase in the order methyl $<$ ethyl $<$ iso-propyl $<$ *tert*-butyl (Matsumura and Yamada 1995). This order is opposite of that found for the ionization energy calculated when solvation is absent: methyl $>$ ethyl $>$ iso-propyl $>$ *tert*-butyl (Baciocchi and Gerini 2004).

It should also be borne in mind that cation-radicals are strong Lewis acids and can act as acceptors of the nucleophile electron pair to form a coordinative bond. Such a process was well documented (Gould et al. 2003, references therein). The Lewis-type binding of water by the aminosilane cation-radical appeared to be crucial for fragmentation with the formation of an α-amino carboradical. The latter plays an important role in the efficiency of photographic systems. Scheme 5.18 illustrates this coordinative-promoted fragmentation of the cation-radical.



SCHEME 5.18

5.4.2 Dynamic Effects

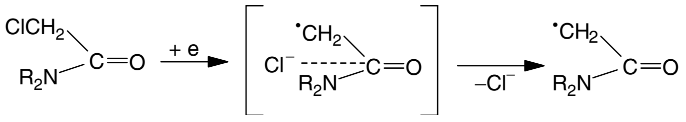
Solvent dynamics controls the rate of electron transfer and sometimes the rate of further transformation of the ion-radicals formed. Generally speaking, solvent effects can be understood as contribution from the solute-solvent dynamic interaction as well as from the alteration of the solvent structure induced by the solute. An electron transfer occurs momentarily between the neighboring molecules. No nuclear motions in the molecules occur during this transfer. (The Franck–Condon principle: Transfer of an electron takes place much faster than nuclear movements.) Therefore, such a rapid electron transfer may take place only when geometry of the ion-radical, at the moment of incipiency, is similar to that of the parent molecule (Warman 1982). Solvent relaxation is assumed to be much faster than electron transfers (Heitele 1993). This means small amplitude motions of an individual solvent molecule experience only weak friction with the surrounding liquid. The barrier to electron transfer arises primarily from the need to reorganize the electron distribution within the reactants and the surrounding solvent before the redox reaction. Once an electron transfer has occurred, excess energy is dissipated fast enough to trap the system on the product side. For weak frictional or random forces, the system undergoes several oscillations between the reactant and the product wells before finally settling down in one of the wells. The reaction rate is limited by how fast the necessary activation energy is acquired and how fast excessive energy is dissipated to trap the system in either well.

5.4.2.1 Solvent Reorganization

Bimolecular electron-transfer reactions in solutions frequently have rates limited by the diffusion of the donor and acceptor molecules, because one or both of the reactant species is usually at a low concentration relative to the solvent. To obtain a detailed mechanistic and kinetic understanding of electron-transfer reactions in solutions, chemists have devised ingenious schemes in which the two reactants, the donor and acceptor, are held in a fixed distance and orientation so that diffusion will not complicate the study of the intrinsic electron-transfer rates. Recent developments, however, have led to theoretical models in which the orientation and the distance are changeable (see Rubtsov et al. 1999).

For an electron transfer to take place, the energy levels of the donor and the acceptor must match. In other words, the donor, the acceptor, and their solvate shells must have a configuration that fits the equilibrium state of the product system (e.g., see Guldi et al. 2001). According to Marcus (1964) theory, such a balance is attained by bond and solvent reorganization. The bond and solvent reorganization energies are denoted as λ_i and λ_o (after inner and outer). The sum of λ_i and λ_o is λ, the reorganization energy. Bond reorganization involves bond stretching or compression, angle deformation, and the changing of torsion moments. Solvent reorganization involves induced changes in the electrostatic environment around the reactants. In ion-radicals with effective spin delocalization (such as in the aromatic species), little molecular deformation occurs and λ_i is small. In this case, λ_o is the most important contribution to the intrinsic barrier of the reaction. However, λ_i value increases when the one-electron transfer leads to ion-radicals that undergo bond fragmentation.

Marcus theory was crucial in the development of electron-transfer studies. It created indispensable demands for reliable magnitudes of standard potentials and reorganization energies. It allowed calculating electron-transfer rate constants and comparing them with the experimental values. In Marcus theory, logarithm of the electron-transfer rate (log k_{ET}) is related parabolically to the driving force of electron transfer between electron donors and acceptors (negative free energy change of electron transfer, $-\Delta G_{ET}{}^0$), and the reorganization energy of electron transfer (λ). If $-\Delta G_{ET}{}^0$ increases, log k_{ET} also increases. At the point of $-\Delta G_{ET}{}^0 \cong \lambda$, log k_{ET} reaches a maximum. After that, the new region begins for which $-\Delta G_{ET}{}^0 > \lambda$. This is the so-called Marcus inverted region. It should be noted that the Marcus theory was developed for electron transfer reactions of metal complexes under conditions of weak interaction between electron donors and acceptors. In the course of organic reactions, however, electron transfer is usually accompanied by transient chemical bonding and strong donor–acceptor interaction.



SCHEME 5.19

Phenomena occurring in solutions include effects of solute–solvent interaction (solvation) and solvent–solvent reorganization (solution restructuring). The overall solvent reorganization energy involves changes in dipole and density components. This concept was introduced by Matyushov (1993) and is developed up to now (Widom and Ben-Amotz 2006). If the solvent and solute polarizabilities are taken into account, it stems notable deviation from the standard free-energy parabolas (Small et al. 2003). The latter authors proposed a new three-parameter electron-transfer model that provides the accurate free-energy surfaces.

What may also be missing in the electron-transfer model is the interaction between the fragments resulting from the one-electron dissociative cleavage. According to Pause et al. (2001, 2002), such an interaction persists even in very polar solvents. The effect was observed for chloride and the trichloromethyl or *p*-cyanobenzyl radical arising from dissociation of the anion-radicals of carbon tetrachloride or *p*-cyanobenzyl chloride in the solution of dichloroethane, DMF, ethanol, and formamide. Cage effect is the problem to be taken into account. Costentin et al. (2005) illustrated the importance of cage effect with the heterogenous (electrode) one-electron reduction of chloroacetamides in DMF. The reduction results in the carbon–chlorine cleavage. However, the chloride formed is held in the solvent cage at the expense of electrostatic interaction with the positive end of the carbonyl dipole (see Scheme 5.19). The authors define the whole process as sticky dissociative electron transfer. The sticky dissociative electron-transfer model was also working well when the kinetic analysis was applied to homogeneous reduction of haloacetonitriles by electrogenerated aromatic anion-radicals in DMF (Isse and Gennaro 2004).

Last time, electron-transfer reactions were frequently performed in micellar media. Analyzing temperature effects on electron transfer from aromatic amines to coumarins in aqueous Trilon X-100 micelles, Kumbhakar et al. (2006) deduced that the two-dimensional electron-transfer (2DET) model is more suitable to explain the results obtained than the conventional electron-transfer theories. The model is detailed in the article by Kumbhakar et al. (2006) and references therein.

The solvent reorganization energy is lesser and the electron transfer is faster when the charge of the electron-transfer product is delocalized more. Even such a weak interaction as hydrogen bonding involving the anion-radical helps to delocalize the charge, thereby decreasing the solvent-reorganization energy and increasing the electron-transfer rate. For example, the formation of the van der Waals (hydrogen-bonded) complex between urea and 4-nitroaniline accelerates the nitro compound one-electron reduction in CH_2Cl_2 by 1 order of magnitude (Bu et al. 2005). The same effect was observed for the one-electron oxidation of 1,1′-bis[(6-methylpyrid-2-yl)aminocarbonyl]ferrocene in CH_2Cl_2 when hydrogen bonding with barbital takes place (Westwood et al. 2004; see also Chapter 8 of this book).

Within Marcus theory, the solvent is described by using the dielectric continuum model. Continuum model remains, even at present, the most developed and common tool for estimating the solvent effect. Nevertheless, the dielectric continuum model is an oversimplification. It does not take into account the molecular nature of the solvent. Particularly, it is not appropriate for ion-radical reactions in nonpolar solvents and it is not able of taking into account the internal polarization of a nonpolar medium. In this connection, both principal advantages of the continuum model and attempts to generalize the theory are noteworthy (Tachiya 1993, Leite 1999, Leontyev and Tachiya 2005, Li and Fu 2005). The approaches mentioned take into account the anisotropic polarizability of the nonpolar solvents and solvent dynamics on a very high-dimensional surface. Models including energy correlation leads to a single collective reaction coordinate. These models recover the Marcus theory when they are combined with the potential difference distribution calculated on the basis of the dielectric continuum model.

Depending on the solvent polarity and redox potentials of a donor and an acceptor, the ions resulting from electron transfer may remain associated either as a contact IRP or as a solvent-separated IRP. In the contact pair, back electron transfer can take place. For such electron back-transfers, the solvent reorganization energy is less than 5% of the total reorganization energy (Serpa and Arnaut 2000).

In general, however, solvent polarity is favorable for an electron transfer. The solvent reorganization energy is particularly large for small ions in polar solvents and is usually low in low-polarity solvents. Therefore, the low polarity of a solvent cannot prevent electron transfer in all of the cases when there is a significant difference between the donor IP and the acceptor electron affinity. Moreover, fragmentation of an ion-radical results in the formation of a neutral radical and a small ion (e.g., $H_3CBr^{-\bullet} \rightarrow H_3C^{\bullet} + Br^-$). The size of Br^- is smaller than that of the initial anion-radical $H_3CBr^{-\bullet}$. The smaller size of the charged species is favorable for solvation. Solvation accelerates the fragmentation reaction. As a result, a decrease in the solvent polarity increases anion-radical stability. For comparison between calculated and experimental data on anion-radicals of halogenated compounds in nonpolar solvents, see Matchkarovskaya et al. (1995) and Shimamori et al. (1993).

Solvent reorganization energy should be taken into account when, during the reaction, a charge moves from one to another portion of the molecule. For instance, in the acetophenone series, such charge transfer takes place according to the following sequence:

$$RC(=O)CH_2X + e \rightarrow RC^{\bullet}(-O^-)CH_2X \rightarrow RC(=O)CH_2X^{-\bullet} \rightarrow RC(=O)CH_2^{\bullet} + X^-$$

Once the initial anion-radical is formed, the solvent is organized around a negative charge, which is mostly concentrated on the carbonyl oxygen. Then the solvent has to reorganize around the negative charge that develops on the leaving group during the reaction. According to estimations by Andrieux et al. (1996), the solvent reorganization contributes 75–100% to the total of the intrinsic energy barrier for the reaction. At the same time, the intrinsic solvation of the developing halide ion disfavors the carbon–halogen cleavage because ordering of the medium increases (i.e., via the entropy term). Moreover, there is a significant attractive interaction between a developing halide and a carboradical, as depicted in Scheme 5.19. To defeat these two restrictive factors (medium ordering and interaction between resulting fragments), strong fugacity of the leaving group and enough polarity of the solvent are needed. An example: In strong polar mediums, solvation of the leaving anion does not determine the kinetics of the chloride elimination from the 4-chlorobenzophenone anion-radical (Jaworski and Leszczynski 1999).

5.4.2.2 Solvent Polarity and Polarization

The buzzword "polarity," derived from the dielectric approach, is certainly the most popular word concerning solvent effects. (It is the basis for the famous rule of thumb *similia similibus solventur*, i.e., "like dissolves like" in English.) We should add "like helps like." Let us compare toluene and *n*-hexane as solvents. At temperatures when both solvents have comparable viscosity, the reaction between 1,2,4,5-tetrafluorobenzene and its anion-radical proceeds in different ways (Werst 1993), depending on the solvent. In toluene, the reaction consists of electron exchange:

$$C_6H_2F_4 + (C_6H_2F_4)^{-\bullet} \rightarrow (C_6H_2F_4)^{-\bullet} + C_6H_2F_4$$

In *n*-hexane, dimerization takes place:

$$C_6H_2F_4 + (C_6H_2F_4)^{-\bullet} \rightarrow (C_6H_2F_4)_2^{-\bullet}$$

Hence, in toluene, no dimer anion-radicals are observed. Encounters between anion-radicals and neutral molecules result in electron transfer instead. Charge transfer from the solute anion-radicals to toluene is unlikely, since toluene is a poor electron acceptor. Consistent with this fact, no differences were observed in the anion-radical ESR-coupling constants in toluene when compared to those in *n*-hexane (Werst 1993). Charge (not electron) transfer from the toluene molecules to the

neutral tetrafluorobenzene is more plausible. However, spectroscopic studies show that such charge transfer is weak. Ion-dipole interactions are insignificant, since the dipole moment of *n*-hexane is near zero and the dipole moment of toluene is negligibly small (0.36 D). Comparing the situation in *n*-hexane, the author surmises that the described solvent dependence is attributable to greater polarizability of the ring-electron system in the toluene solvent molecules in the presence of anion-radicals (Werst 1993).

The solvent effects in nonpolar solvents described earlier are not limited to anion-radicals solely. A cation-radical example is the tetramethylethylene cation-radical, $(Me_2C{=}CMe_2)^{+\bullet}$. Like $(C_6H_2F_4)^{-\bullet}$, $(Me_2C{=}CMe_2)^{+\bullet}$ reacts with the neutral $Me_2C{=}CMe_2$ molecule to form the ion dimer (and also high-order aggregates) in the alkane solutions, but not in toluene. Electron donor–acceptor interactions between $(Me_2C{=}CMe_2)^{+\bullet}$ and the solvent molecule can be ruled out because the ESR parameters of this cation-radical are same in alkanes and toluene (Werst 1993). Then, the greater polarizability of arenes as compared to alkanes leads to a stronger interaction between ion-radicals and solvent molecules. This in turn prevents dimer formation between neutral molecules and their ion-radicals in arene solvents. Electron-exchange reactions between these solutes take place instead of dimer formation. We see a close parallel in polarizability effect on the outcome of cation-radicals as anion-radicals.

Potvin et al. (2003) focused their attention on one special but principal case of the solute influence on the solvent polarization. Considering electron transfer between donors and acceptors in acetonitrile, the authors observed the following: The donors bearing carboxylic groups were more active than their noncarboxylic analogs. The finding is consistent with ionization of the COOH group and electrostatic promotion of electron transfer. Even a single COO^- substituent suffices to provide such assistance: It defines a spherical "bubble" of electrostatically attractive space to facilitate electron transfer.

5.4.2.3 Solvent Internal Pressure

At least in the outer-sphere ion-radical reactions, a reactant and a substrate form a CTC. Then ion-radicals are formed and released. Then some chemistry takes place. In other words, there are several intermediate states in ion-radical organic reactions and in each state, the size of the structure is not small. Therefore, each state needs an appropriate hole in the bulk solvent. Some authors indicate that mechanism of electron transfer involves a gradual electron shift from donor to acceptor. This shift is conjugated with simultaneous reorganization of the reactants and media, rather than an electron jump after preliminary reorganization (see, e.g., Kuzmin 1996). It is obvious that for the dissolution of a substance in a solvent, a hole (cavity) must be created within the solvent to accommodate the new solute. The translational motion of any species in a liquid is possible only when sufficient free volume is available. The formation of free volume certainly requires the expenditure of energy. The amount of the energy expended will depend on the magnitude of the intermolecular forces of attraction between the solvent molecules on one hand and between the solvent and solute molecules on the other. Viscosity of the solvent is also important in this sense. At this point, the relationship between viscosity and results of cation-radical rearrangements should be emphasized (see a review by Adam and Trofimov 2003). Intrinsic volume of the solvent molecule must also be taken into account. To illustrate, it is proper to compare acetonitrile and propylene carbonate, both of which are typical solvents. Although acetonitrile is linearly shaped, propylene carbonate (4-methyl-1,3-dioxolan-2-one) has a five-membered ring with a methyl substituent. It is clear that compressibility of acetonitrile must be larger than that of propylene carbonate. This difference reflects in the kinetics of the one-electron transfer from the *N*,*N*′-dibenzyl-4,4′-bipyridine cation-radical to *N*,*N*′-dibenzyl-4,4′-bipyridinium (Shihab et al. 2004).

By and large, the solute exerts "pressure" on the solvent. Internal pressure can affect the liquid-phase ion-radicals reactions and requires special study. For instance, such pressure can determine the selectivity and even the stereochemistry of these reactions (Okamoto et al. 1998, Adam and Trofimov 2003).

5.4.2.4 Solvent Conformational Transition

Some organic ion-radical reactions can be initiated by laser photolysis or pulse radiolysis. The main result of these processes consists in the generation of the thermalized electron (e_t) and the solvent hole ($RH^{+\bullet}$). The e_t is usually scavenged by means of small amounts of additives such as haloalkanes (e.g., carbon tetrachloride), or electrophilic gases (carbon dioxide, nitrous oxide, etc.). The solvent hole, that is, $RH^{+\bullet}$, inevitably plays a role in electron transfer with the participation of an organic substrate. Essentially, the solvent molecules stay in the cation-radical state for some time. Let us consider two conventional solvents for such reactions, cyclohexane and decalin. According to Shkrob et al. (1996a, 1999), Shkrob et al. (1996b), and Sauer et al. (1996), these two solvents produce quite different kinetics of electron-transfer reactions.

At 25°C, the cyclohexane molecules mainly have the chair form. The equilibrium concentration of the isomeric twist form is $\sim 10^{-4}$ mol · dm^{-3}. On ionization, the solvent cation-radicals in the chair form are predominant. Electron transfer between the chair form of the cyclohexane cation-radicals and the chair-shaped surrounding cyclohexane (neutral) molecules is very fast, since it requires minimum reorganization energy. However, the chair-form cation-radical sometimes approaches a minor part of the neutral molecules in the twisted form. Because the twisted cyclohexane has lower IP, the twist-shaped molecules scavenge the cation-radicals in the chair form.

Once formed, the twisted cation-radical become surrounded by the chair-form neutral molecules. It does not transfer the hole to the neighboring chair-form neutral molecules until this twisted cation-radical acquires the chair configuration in a spontaneous manner. As a result, fast migration of the hole, that is, the one-electron transfer from the neutral solvent molecule to its cation-radical, is detained. Hummel and Luthjens (1986) considered the idea that conformation dynamics is involved in the electron transfer. Scheme 5.20 illustrates this dynamics.

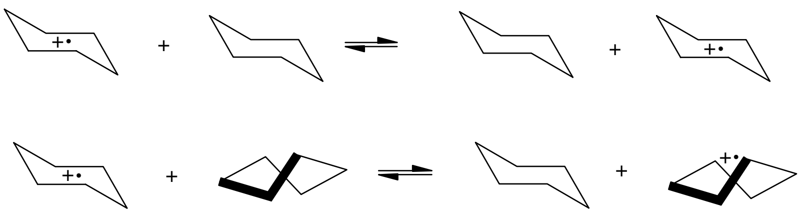
As noted, the twisted conformer, which has a lower IP, rapidly scavenges the chair form of the cation-radical. Being endothermic, the backward transfer is relatively slow, and equilibrium is reached in 20–30 min. Thus, the electron transfer can be described as a series of periods of very fast hole migration between the chair forms and intermittent migration with the participation of the twist forms.

It is important that both the twisted and chair forms of the cylclohexane cation-radical react with a solute, for example, with perylene. Therefore, generation of the perylene cation-radical is characterized with bimodal kinetics under these conditions.

No such confusion arises for decalins. In decalin mixtures, a reversible electron-transfer reaction takes place:

$$cis\text{-decalin} + (trans\text{-decalin})^{+\bullet} \rightarrow (cis\text{-decalin})^{+\bullet} + trans\text{-decalin}$$

Because of the high concentration of isomeric molecules (>0.1 mol · dm^{-3}), this equilibrium is established instantaneously. The IP of *trans*-decalin is 0.02 eV lower than the IP of *cis*-decalin (9.24 eV versus 9.26 eV). Therefore, the electron-transfer equilibrium is shifted slightly to the left side. Thus, in terms of charge-transfer kinetics, the two ions behave as a single species. It should be worth noting that decalin has only two isomeric forms, cis and trans. On the contrary, *n*-nonane exists in the multitude of conformations. The rate constant of electron exchange between parent neutral molecules of nonane and its cation-radicals is much lower, namely, 2 orders lower than the diffusion-controlled limit (Borovkov et al. 2007).



SCHEME 5.20

As we have seen, both cyclohexane and decalin are a binary mixture of conformers. As discussed earlier, it is obvious that conformers of the decalin cation-radical act in parallel, whereas conformers of the cyclohexane cation-radical have quite different kinetics of their reactions with uncharged molecules of a solvent and a solute.

Considering nonequilibrium configurations of the solvent and the solute in electron transfer, some authors note that the solvent hole should be suitable to accommodate an ion-radical salt when the counterions are kept with each other. For example, the intermolecular electron transfer between the coumarin-337 solute and the *N*,*N*-dimethylaniline solvent results in solution anisotropy. The anisotropy indicates that the donor and acceptor molecules are aligned with their long axes that are roughly perpendicular. The donor (dimethylaniline) and the acceptor (coumarin) have ground-state dipole moments of 1.6 D and 10.0 D, respectively, and align roughly along their long axes. Electron transfer is rate-controlled by a favorable overlap of the corresponding occupied and vacant MOs. The mutual orientation of the resulting counterions dictates hole size and shape in the solvent (Akhremitchev et al. 1999).

Solvent polarization can also play a role in the stabilization of conformationally nonuniform particles. For example, 4-(1-phenylpiperidin-4-ylidene) cyclohexylidene propanedinitrile transforms into completely charge-separated species on photoirradiation. This species contains the C=C bond and bears two ion-radical centers: $N^{+\bullet}$ and $C^{-\bullet}$. As explained (Hoogesteger et al. 2000), the species formed keeps a folded conformation in cyclohexane and a stretched conformation in benzene.

5.4.2.5 Solvent Temperature

Temperature effect on ion-radical stability and the very possibility of ion-radical organic reactions have already been discussed in the preceding chapters. However, one topic of the problem deserves a special consideration, namely, the effect of solvent temperature on dynamics of IRPs. In a definite sense, IRPs are species close to CTCs. As known, the lower the medium temperature, the higher is the stability of CTCs. And what about IRPs?

Karasawa et al. (1971) established that the anion-radical of biphenyl or naphthalene forms an ion pair in THF solution in the presence of a sodium cation. THF has a dielectric constant of 7.6 (only after $\varepsilon = 10$, a solvent becomes dissociating). In THF, ion-radicals remain essentially associated with their counterions. At 20°C, tight pairs of the biphenyl and naphthalene anion-radicals with sodium cations dominate, although the loose ion pairs are the most abundant at the lowest temperatures. Hence, lowering the temperature decreases the stability of tight ion pairs containing organic ion-radicals. This unusual regularity is explained (Smid 1972) by certain thermal effects. In ethers (THF is an ether), formation of separated ion pairs is usually exothermic. Selective ion-solvent interaction contributes significantly to the exothermicity of the ion-pair separation in ethereal solutions. A temperature decrease assists in heat dissipation and facilitates this ion-pair separation. In addition, a temperature decrease causes an increase in the dielectric constants of polar solvents. Polar-solvent molecules have dipole moments. A dipole order–disorder transition takes place in the course of thermal movement. The lower the temperature, the greater is the regularity of disposition of solvent molecules, and the higher the dielectric constant. This phenomenon also contributes to ion-pair loosening. Association into an ion pair tends to reduce reactivity of the ion. The higher the loosening of ion pairs, the lower is the diminution of their reactivity. The rate and the state of equilibrium of electron-transfer reactions also depend on the association of the resulting ion-radicals with counter ions.

So the temperature decrease results in an increase in the dielectric constant of the liquid polar solvent. However, freezing a solvent has the opposite effect. On freezing with glass formation, the effective solvent dielectric constant decreases drastically, because the solvent dipoles cannot reorient. The frozen glass, therefore, cannot stabilize the newly formed ions (Liddell et al. 1997).

5.4.3 Liquid Crystals and Ionic Liquids as Solvents

Liquid-crystalline media are important especially for technical and biomedical applications of electron-transfer reactions. Molecular electronic systems, photosynthetic processes, and some

enzymatic transformations proceed in liquid-crystalline media. The generally observed trend is significantly lower kinetics, even a dynamical arrest of electron transfer in liquid-crystalline solvents relative to isotropic solvents of comparable polarity. The isotropic-nematic transition leads to weak discontinuities of the solvation energy (at the transition point) and appearance of the solvation anisotropy. Accordingly, the reorganization energy shows a significant anisotropy with respect to the orientation of a donor–acceptor complex relative to the longer axis of the liquid-crystalline solvent molecule (Lilichenko and Matyushov 2003). All changes to the reaction barrier at the transition point are related to anisotropy of the solvation energy in the nematic phase. The anisotropy is mostly a result of microscopic correlations of solvent dipoles (Kapko and Matyushov 2006). Liquid crystals as solution media seem to be an intriguing area, but what we need to know far exceeds what is known now. Advanced research efforts would be very desirable in this field. One of the important steps is represented by a review by Matyushov (2007).

Ionic liquids have been proposed as solvents for green-processing chemical reactions. An ionic liquid is a liquid containing only ions, but it is different from a molten salt. Ionic liquids are usually composed of organic cations such as quaternary ammonium, imidazolium, and pyrrolidinium as well as cations from heterocyclic aromatic and nonaromatic compounds or derivatives of natural products, alkylammonium and some other task-specific cations. Nitrate, tetrachloroaluminate, tetrafluoroborate, hexafluorophosphate, triflate, bistriflatoiminate, and dicyanoimidate are used as anions. These highly asymmetric, bulky cations and anions are hardly packed in the crystal lattice and comprise liquids at room temperature. Their properties can be tuned by a mix design in appropriate cations and anions. Of course, ionic liquids are not the same solvents that can be applicable if very low temperature is needed for an ion-radical organic reaction. For instance, 1-ethyl-3-methylimidazolium dicyanoimidate has a melting point of −21°C (MacFarlane et al. 2002).

Ionic liquids are used more as solvents in the normal-temperature homogeneous, heterogeneous, or pulse-radiolysis processes (see, e.g., Lagrost et al. 2003, Skrzypczak and Neta 2003). Therefore, it is meaningful to discuss the specificity of ionic liquids as reaction solvents. In chemical technology sense, their properties such as chemical stability within a large temperature range, nonvolatility, low flammability, high electric conductance, and broad electrochemical window are attractive. We should scrutinize properties of ionic liquids that are specifically important for electron transfer and for the outcome of the ion-radicals formed. Specificity of ionic liquids as solvents for radiolytic generation and spectroscopic characterization of organic ion-radicals has already been considered earlier.

Ionic liquids are relatively viscous and dynamics of its reorganization is very slow. The very initial step of ion-radical reactions—the formation of encounter complexes between a donor and an acceptor—has the diffusion nature. This step can be hindered in ionic liquids. The next step of the intimate electron-transfer mechanism consists in the formation of an electron-overlap complex, that is, a CTC. After that, separation of the single-unit charges takes place with loosening of ion-radical counterparts that formerly composed CTC. High viscosity of ionic liquid impedes ion-pair separation. The higher the viscosity of the ionic liquid, the slower is the rate of the electron-transfer process. Generally, ionic liquids are basically restricted systems resembling zeolites. The higher ionizing power of ionic liquids as compared to aprotic molecular solvents favors the slow but progressive transformation of CTC complex into an IRP. It was in ionic liquid solutions that CTC of tetracyanoetylene with Michler's ketone gave rise to the corresponding anion- and cation-radical (Chiappe and Pieraccini 2006). (Michler's ketone is 4,4′-bis(dimethylamino)benzophenone.)

Further, the cationic parts of some ionic liquids possess a donor or an acceptor H-bond ability. For example, 1-ethyl-3-methylimidazolium is capable of forming hydrogen bonds with the participation of all the three-ring hydrogen atoms, at second, fourth, and fifth positions (Elavi et al. 1995). If the resulting ion-radical bears fragments that are prone to form hydrogen bonds, the electron-transfer reaction receives an additional driving force. However, possibility of the 1,3-dialkylimidazolium salt to expel proton from the second position and to form a stabilized carbene must be taken into account. This deprotonation proceeds even in the presence of moderate bases

(Handy et al. 2006). Anion-radicals are bases and their basicity is frequently very high. When the anion-radicals are formed in alkylimidazolium ionic liquids, there is some danger of their undesirable protonation.

The one-electron oxidation of aromatic substrates can be facilitated in the alkylimidazolium salt solutions by significant stabilization at the expense of π–π solute–solvent interaction (Brooks and Doherty 2005). Polarity of ionic liquids is also a favoring factor, but this polarity is close to that of normal polar organic solvents. According to estimations, ionic liquids are more polar than acetonitrile and less polar than methanol (Reichardt 2005, 2007).

In the light of all these regularities, it is interesting to compare the outcomes of two anion-radicals, from 4-chlorobenzene and 9-chloroanthracene, generated electrochemically in ionic liquid media (Lagrost et al. 2004). The authors studied kinetics of the carbon–halogen bond cleavage in the anion-radicals mentioned. When the charge and spin are spread out over the entire carcass as in the 9-chloroanthracene anion-radical, an acceleration of the carbon–halogen bond cleavage is observed in ionic liquids as compared to the kinetics of the same cleavage in acetonitrile. On the contrary, in the case of 4-chlorobenzophenone anion-radical with the charge and spin more localized on the oxygen atom of the carbonyl group, a large decrease of the C–Cl cleavage kinetics takes place in the ionic liquid media. The earlier-mentioned specificity of ionic-liquids as solvents makes these kinetic effects completely understandable.

One more difference between ionic liquids and conventional organic solvents of the C–Cl cleavage should be mentioned. Normally, the intrinsic solvation of the developing halide ion disfavors the cleavage via the entropy term. Such a term cannot be significant in the ionic liquids composed of very bulky cations and anions.

5.5 SALT EFFECTS

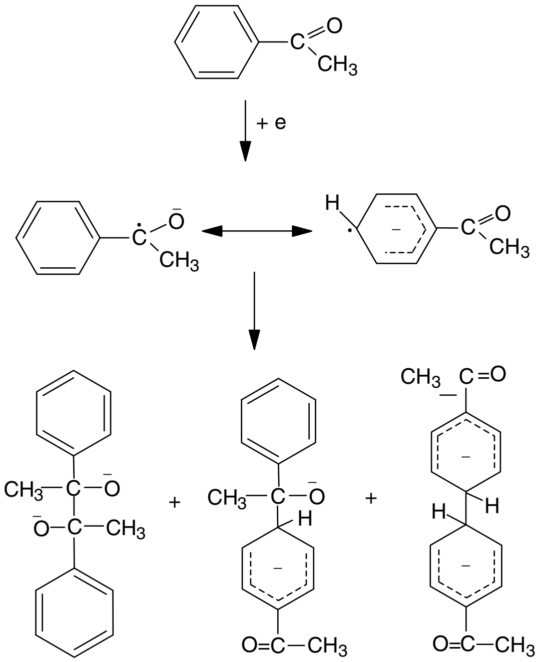
5.5.1 Salt Effect on Spin Density Distribution

On one-electron reduction, aldehydes and ketones give anion-radicals. It is the carbonyl group that serves as a reservoir for the unpaired electron: Ketones yield pinacols exclusively. Thus, acetophenone forms 2,3-diphenylbutan-2,3-diol as a result of electrolysis at the potential of the first one-electron transfer wave (nonaqueous acetonitrile as a solvent with tetraalkylammonium perchlorate as a supporting electrolyte) (van Tilborg and Smit 1977). In contrast, calculations have shown that the spin densities on the carbonyl group and in the para position of the benzene ring are equal (Mendkovich et al. 1991). This means that one should wait for the formation of three types of dimer products: "head-to-head," "tail-to-tail," and "head-to-tail" (cf. Section 3.2.1). For the anion-radical of acetophenone, all of the three possible dimers are depicted in Scheme 5.21.

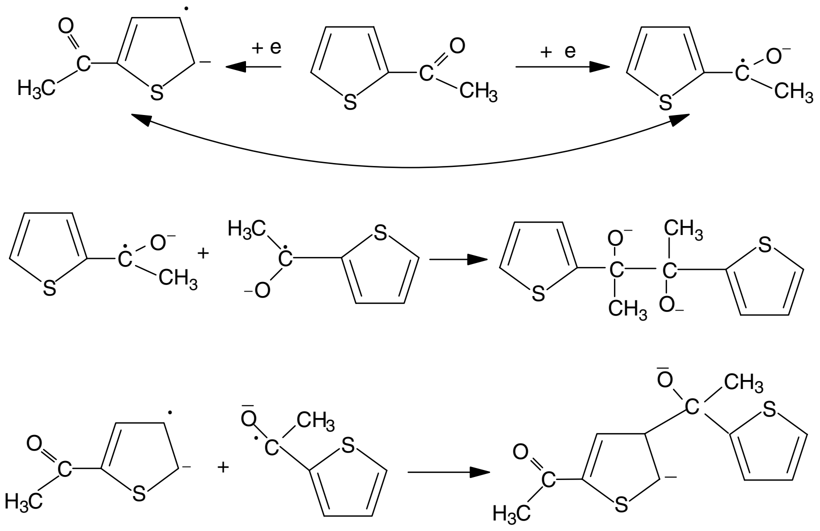
For this section, yield of the "head-to-head" product is relevant. In DMF with 0.1 M of tetrabutylammonium perchlorate, electrolysis of acetophenone at the potential of the first one-electron wave produces this dimer in 30% yield. This is in accord with the earlier-mentioned prediction that all the three directions of this dimerization are equally probable. If lithium perchlorate is the supporting electrolyte in the same solution, the "head-to-head" dimer yield rises to 70% (Gul'tyai et al. 1987a). Hence, "head-to-head" coupling becomes the main route of dimerization.

In the case of the "free" 9-acetylanthracene anion-radical, the spin density on the carbonyl group is lower than that in the para position (position 10) by a factor of 5. The formation of the "tail-to-tail" dimer should be expected. Actually, preparative reduction of 9-acetylanthracene in DMF against the background of a tetrabutylammonium salt results in the "tail-to-tail" dimer with the yield of 70%. Addition of a lithium salt, however, decreases the dimer yield to 45% (Gul'tyai et al. 1987b, Mendkovich et al. 1991).

It is interesting to compare yields of the "head-to-head" diol from 2-acetylthiophene in their dependence on the composition of the reaction medium (DMF as a solvent). This diol is formed in 10–15% yield with 0.1 M of Bu_4NClO_4, in 42% yield with 0.1 M of Bu_4NClO_4 + 0.01 M of $LiClO_4$,



SCHEME 5.21



SCHEME 5.22

and in 62% yield with 0.1 M of $LiClO_4$ (Gul'tyai et al. 1988). For 2-acetylthiophene, Scheme 5.22 demonstrates the formation of the "head-to-head" and "head-to-tail" dimers.

From all of the quoted data, the addition of lithium perchlorate results in the formation of ion pairs, that is, lithium-ketyls. This helps in displacing the spin density toward the carbonyl group. The lithium cation has high affinity to the "hydroxy anion" in the ketyl fragment (interaction between two hard ions, O^- and Li^+). Such affinity prevails over the ion-pair disrupting power of DMF, which has a high dielectric constant ($\varepsilon = 37$, very far from the threshold of $\varepsilon < 10$ for nondissociating

solvents). Meanwhile, the marked dependence of yields of the “head-to-head” product on the concentration of lithium perchlorate means that the tight ion pair with spin localization on C=O is in equilibrium with the more or less free anion-radicals. According to the usual rule of equilibrium shift, the percentage of $Th–C^{\bullet}–O^{-}$, Li^{+}, that is, thiophene lithium-ketyl tight pair, should increase as the concentration of $LiClO_4$ increases.

$$Th–C^{\bullet}–O^{-}//Bu_4N^{+} + Li^{+}ClO_4^{-} = Th–C^{\bullet}–O^{-}, Li^{+} + Bu_4N^{+}ClO_4^{-}$$

The addition of sodium iodide to a solution of the camphoroquinone anion-radical sodium salt results in enhanced ion association. This association pulls spin density onto oxygen. Stevenson et al. (1998) used the camphoroquinone *R*- or *S*-conformer for the anion-radical preparation in the chiral solvent [*SS*- or *RR*-2,3-dimethoxy-1,4-bis(dimethylamino)butane]. In this case, the interaction of the chiral-solvated cation with the chiral anion-radical (semidione) results in specific line broadening in ESR spectra. This opens a new approach to the ESR chiral discrimination of the semidiones in a chiral solvent (solvent—ion-pair chiral recognition). Diastereotopic-solvated ion pairs that form and dissociate rapidly on the ESR time scale produce some asymmetry in the spectrum. As known, chiral-shift reagents perturb the NMR chemical shifts of each enantiomer differently and allow for chiral resolution. A significant difference in the ESR experiments described by Stevenson et al. (1998) and the use of NMR chiral-shift reagents comes from the fact that the ESR chiral-shift reagent is the solvent itself. Obviously, similar effects can be observable for other ion-radicals with counterions surrounded by other chiral solvents.

Anion-radicals of arylalkenyl sulfones also dimerize during electrochemical generation in aprotic solvents in the presence of lithium salts as supporting electrolytes. The corresponding symmetric carbon–carbon dimers are formed in high (up to 80%) yields. Importantly, in the presence of tetraalakylammonium instead of lithium salts, the whole process is directed toward polymerization at the expense of the vinyl fragment (Delaunay et al. 1995). Salt effects considered in this section consist of the formation of contact ion pairs between alkali cations and anion-radicals bearing polar fragments. Ion pairing causes redistribution of the frontal electron density and leads to its localization on a polar group or next to such a group in the case of vinyl derivatives. In its turn, this phenomenon results in suppression of polymerization and assists in the dimer formation.

5.5.2 Salt-Cage Effect Interplay

Solvent-cage effect plays an important role in the outcome of incipient organic ion-radicals. Salts can seriously change the influence of the cage effect on the reactivity of IRPs. In this connection, let us consider one more example concerning the reduction of carbonyl compounds giving some turn in the salt-effect theme. Shaefer and Peters (1980), Simon and Peters (1981, 1982, 1983, 1984), Rudzki et al. (1985), and Goodman and Peters (1986) described photoreductions of aromatic ketones by amines. In this case, adding excess $NaClO_4$ results in considerable retardation, even prevention, of final product formation. The two fundamental steps in this photoreduction consist of rapid electron transfer from the amine to the photoactivated ketone (in its triplet state), followed by slow transfer of proton from the amine cation-radical to the carbonyl anion-radical fragment:

$$>C=O + >N^{\bullet\bullet}–CH< \rightarrow >C^{\bullet}–O^{-} + >N^{+\bullet}–CH< \rightarrow >C^{\bullet}–OH + >N^{\bullet\bullet}–C^{\bullet}< \rightarrow \text{Products}$$

The formation of a contact ion pair between the anion-radical and the cation-radical facilitates the proton transfer. This reaction step proceeds in a solvent cage. Adding sodium perchlorate breaks this ion pair up:

$$[>C^{\bullet}–O^{\bullet}, >N^{+\bullet}–CH<] + M^{+}, ClO_4^{-} \rightarrow >C^{\bullet}–O^{-}, M^{+} + >N^{+\bullet}–CH<, ClO_4$$

Solvents, specifically surrounding the sodium cation, lower its effect. In the presence of a crown ether, including and blockading the sodium cation, the rate of the final product formation is entirely restored.

Each cation-radical has a positive charge and an unpaired electron. In the simultaneous presence of an anion (A^-) and a free radical ($R^•$), both of them can attack a cation-radical in a competitive manner. These two possibilities are shown for the example of an aromatic cation-radical ($ArH^{+•}$):

$$ArH^{+•} + A^- \rightarrow Ar^•(H)A \rightarrow ArA + H^•$$

$$ArH^{+•} + R^• \rightarrow Ar^+(H)R \rightarrow ArR + H^+$$

The driving force of the reaction between a radical and an aromatic cation-radical is based on their mutual affinity because both species possess unpaired electrons. There is no coulombic attraction and no coulombic repulsion in this case. The reaction between an anion and an aromatic cation-radical involves electrostatic attraction as the driving force. It necessarily proceeds through a contact (intimate) ion pair $Ar^{+•}$, A^-. It is obvious that disintegration of the mentioned ion pair has to retard or even prevent ArA formation.

Hubig et al. (1994) studied factors that lead to the predominance of the radical or anionic reactions. Three distinct classes of substitution reactivity can be discerned in the halogenation of methyl-substituted methoxybenzenes (ArH) by iodine monochloride (ICl), namely, exclusive iodination, exclusive chlorination, and mixed iodination–chlorination (Hubig et al. 1994). Spectral studies established the prior formation of the CTC [ArH, ICl]. The complex suffers electron transfer to afford the reactive triad ($ArH^{+•}$, $I^•$, Cl^-). Chlorination and iodination result from the quenching of the aromatic cation-radical by chloride ion and iodine atom, respectively. Iodination versus chlorination thus represents the competition between radical- and ion-pair collapses from the reactive triad, and it is predictably modulated by a dissociating ability of a solvent and by adding a "foreign" salt. In nondissociating solvents (CCl_4 and CH_2Cl_2), the collapse of the destabilized ion pair is enhanced and leads to a higher proportion of the chlorinated product. In contrast, when the ions are readily separated and stabilized by solvation with polar solvents such as acetonitrile, the radical collapse becomes predominant making iodination competitive. The ratio [ArI]/[ArCl] is equal to 90/10 in CH_3CN (ε = 36) or 60/40 in CH_2Cl_2 (ε = 8.9). If CH_2Cl_2 contains 0.2 M $Bu_4N^+PF_6^-$, the ratio changes to 40/60. Tetrabutylammonium hexafluorophosphate liberates chloride ion from the reactive triad by preferential ion pairing. Hence, the cation-radical remains approachable for the radical attack.

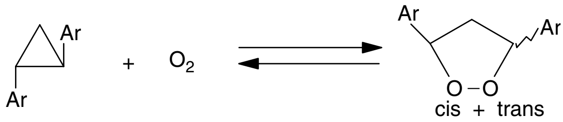
Kochi's group obtained similar results for the reaction between ArH and $C(NO_2)_4$ (Sankararaman et al. 1987, Masnovi et al. 1985, 1989). After photostimulated electron transfer, the related triad was formed

$$ArH + C(NO_2)_4 \rightarrow [ArH^{+•}, {}^•NO_2, {}^-C(NO_2)_3]$$

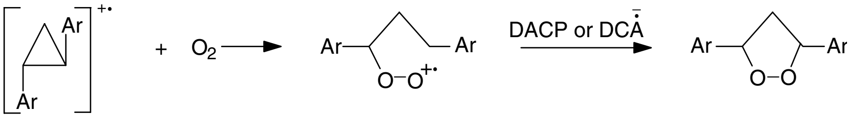
In dissociating solvents, $ArNO_2$ is obtained almost exclusively. In solvents of low dielectric constant, the main product is $ArC(NO_2)_3$. Formation of the latter product is completely prevented on the addition of $Bu_4N^+ClO_4^-$ to nondissociating CH_2Cl_2, whereas formation of $ArNO_2$ is unaffected. Here again, this effect is due to the added salt breaking up the ion pair via an ion-pair exchange process:

$$ArH^{+•}, {}^-C(NO_2) + Bu_4N^+ClO_4^- \rightarrow ArH^{+•}, ClO_4^- + Bu_4N^+, {}^-C(NO_2)_3$$

Considering salt-cage effect interplay, it is necessary to go into a possibility of suppressing back-electron transfer during the formation of ion-radicals. One of the most prominent manifestation of this interplay consists in the oxidation of 1,2-diarylcyclopropane (DACP) with oxygen in the presence of photoexcited 9,10-dicyanoanthracene (DCNA)* in acetonitrile (Mizuno et al. 1987) (Scheme 5.23).



SCHEME 5.23



SCHEME 5.24

If the reaction proceeds in the presence of $Mg(ClO_4)_2$, the product yield becomes significantly better. The added salt suppresses back-electron transfer:

$$DACP + (DCNA)^* \rightarrow [DACP^{+\bullet}, DCNA^{-\bullet}]$$

$$2[DACP^{+\bullet}, DCNA^{-\bullet}] + Mg(ClO_4)_2 \rightarrow 2[DACP^{+\bullet}, ClO_4^{-}] + [2(DCNA^{-\bullet}), Mg^{2+}]$$

After all, the released cation-radical reacts with oxygen according to Scheme 5.23. This reaction was performed in acetonitrile, a solvent of high polarity. For solvents of moderate polarities, the addition of salts, that is, electrolytes increases their polarity (Thompson and Simon 1993). With increased solvent polarity, the electron-transfer rates also increase (Scheme 5.24).

The oxidative photocleavage of 1,2-bis(4-methoxyphenyl)cyclobutane is also accelerated in the presence of $Mg(ClO_4)_2$. However, no salt effect was found for 1,2-diphenylcyclobutane because the high-speed back electron transfer prevents interaction of the caged ion pair with the added salt (Pac et al. 1987).

It is important to differentiate between the effects of a nonnucleophilic salt such as $Mg(ClO_4)_2$ on one hand, and a weak nucleophilic salt such as Et_4NOAc on the other. The effect of nonnucleophilic salts on photo-oxygenation via electron transfer can be understood as the stabilization of ion-radicals by coulombic interaction, resulting in the suppression of a back electron transfer between ion-radicals. The weak nucleophilic salts cause unusual effects. The addition of the anionic nucleophile to the cation-radical and complexation of the weak nucleophilic salt with the ion-radicals bring about these effects.

5.5.3 Salt Effect on Course of Ion-Radical Reactions

The salt effects just considered are counterion effects. Sometimes, however, an added salt can induce electron transfer from a donor to an acceptor. Here are several examples.

Ruiz et al. (1989) studied ligand substitution in transition metal complexes. They found that the presence of a simple sodium salt completely changes the course of these reactions. One of the cases consists in the reaction of Fe(I) sandwiches with PMe_3 in THF. This reaction proceeds only in the presence of a sodium salt.

Without adding this salt, the 19-electron (19e) complex $[(cp)Fe(C_6H_6)]$, cp = η^5-C_5H_5, reacts with PMe_3 in THF at −15°C via hydrogen transfer from THF or PMe_3:

$$[(cp)Fe(C_6H_6)] + PMe_3 \rightarrow [(cp)Fe(PMe_3)_2(H)]$$

In the presence of $NaPF_4$ (1 equivalent), disproportionation occurs under the same reaction conditions. The following two products are formed in equimolecular amounts:

$$[(cp)Fe(C_6H_6)]/NaPF_6 + PMe_3 \rightarrow [(cp)Fe(PMe_3)_3]^+ PF_6^- + (PMe_3)_3Fe(PMe_2CH_2)(H)$$

The replacement of the benzene ligand with PMe_3 results in formations of the 17-electron (17e) complex and then the 19-electron (19e) complex:

$$[(cp)Fe(C_6H_6)] + PMe_3 \rightarrow [(cp)Fe(PMe_3)_2] \text{ (17e)} + PMe_3 \rightarrow [(cp)Fe(PMe_3)_3] \text{ (19e)}$$

The hydrogen abstraction from the medium is one way of stabilizing the 17-electron complex:

$$[(cp)Fe(C_6H_6)] + PMe_3 \rightarrow [(cp)Fe(PMe_3)_2(H)]$$

It is worth noting that THF and PMe_3 are good hydrogen donors. The 19-electron species $(cp)Fe(PMe_3)_3$ is extremely electron rich. It readily reduces the initial complex $[(cp)Fe(C_6H_6)]$:

$$[(cp)Fe(PMe_3)_3] + [(cp)Fe(C_6H_6)] \rightarrow \{[(cp)Fe(PMe_3)_3]^+[(cp)Fe(C_6H_6)]^-\}$$

In the presence of $NaPF_6$, the large ion pair undergoes metathesis and transforms into two smaller ion pairs:

$$\{[(cp)Fe(PMe_3)_3]^+[(cp)Fe(C_6H_6)]^-\} + NaPF_6 = [(cp)Fe(PMe_3)^+\ PF_6^-] + (cp)Fe(C_6H_6)^-Na^+]$$

The stability of (20e) anion $[(cp)Fe(C_6H_6)]^-$ sharply diminishes when this (20e) anion transfers from the salt with $(cp)Fe(PMe_3)_3^+$ into the salt with Na^+. The sodium salt is decomposed easily.

$$[(cp)Fe(C_6H_6)^-\ Na^+] + PMe_3 \rightarrow (cp)^-\ Na^+ + C_6H_6 + (PMe_3)_3Fe(PMe_2CH_2)(H)$$

The decomposition of the salt $[(cp)Fe(C_6H_6)^-\ Na^+]$ displaces the equilibrium with the participation of this salt to the right. Hence, the difference in stability of the (20e) anion $(cp)Fe(C_6H_6)^-$ depending on the cation nature is the major factor responsible for the salt effect. The $NaPF_6$ salt can induce electron transfer between neutral organometallic species very efficiently.

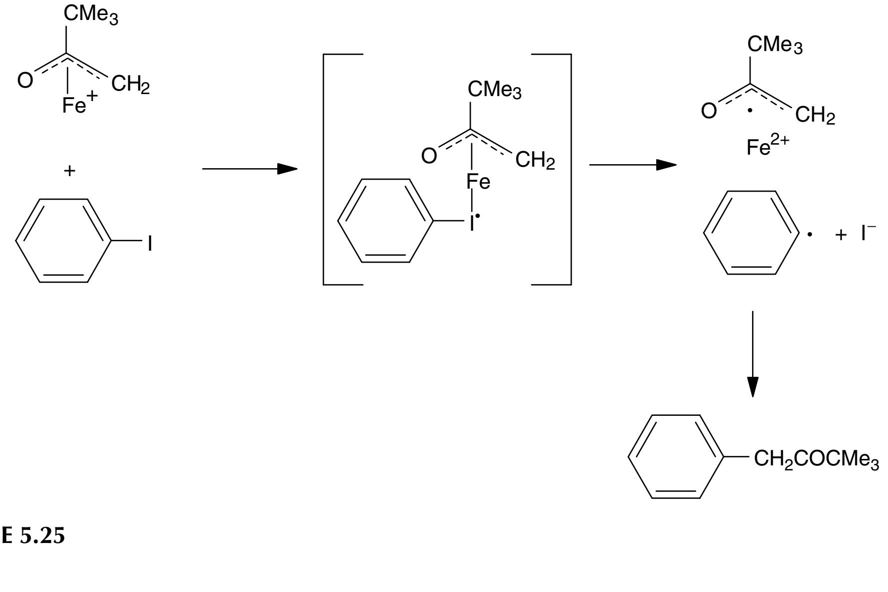
The next example deals with an effect of ferrous chloride addition (Galli and Gentili 1993). Phenyl iodide reacts with the potassium derivative of 1,1-dimethyl-butan-2-one (pinacolin) in DMSO according to the following equations:

$$CH_3COCMe_3 + t\text{-BuOK} \rightarrow t\text{-BuOH} + KCH_2COCMe_3$$

$$PhI + KCH_2COCMe_3 \rightarrow PhCH_2COCMe_3 + KI$$

Without illumination, the reaction proceeds slowly, but by no means it is negligible: 8% of phenylpinacolin is formed, with no regard to the prolonged duration. The addition of ferrous chloride in amounts of 40% to molar equivalent of PhI results in incisive acceleration of this reaction. The disappearance of PhI is observed within 20 min, replaced by 74% of the substitution product, $PhCH_2COCMe_3$, and ca. 10% of the disubstitution product, $Ph_2CHCOCMe_3$. The authors cite diverse data, theorizing that iron(II), associated with the enolate ion, acts as an electron-transfer relay between the enolate and phenyl iodide (Scheme 5.25).

Hence, the addition of $FeCl_2$ eases the electron transfer. As already mentioned, this electron-transfer reaction occurs spontaneously without the addition of the salt, but with lower efficiency. Ferrous chloride sharply increases the reaction efficiency. It is interesting that analogous reaction



SCHEME 5.25

of PhC≡CBr with $PhCOCH_2K$ in DMSO in the presence of $FeCl_2$ gives rise to PhC≡CH only, in quantitative yield. A transfer of one electron initiates the initial debromination, after which further reduction of radical PhC≡C(•) into anion PhC≡C(⁻) takes place. In spite of the difference mentioned in the resulting products, the common feature of these two reactions consists of the necessity in iron(II) ion catalysis for the initial electron transfer (Galli and Gentili 1994).

One surprising example is how ferric (not ferrous) chloride catalyzes the formation of ketyl radicals in a Gringnard-type reaction between $(CH_3)_3CCl$, Mg, and $(CH_3)_2C{=}O$ (Ashby and Wiesemann 1978). The initially formed *tert*-butyl magnesium chloride reacts with ferric chloride and gives *tert*-butyl iron(III) dichloride:

$$(CH_3)_3CMgCl + FeCl_3 \rightarrow MgCl_2 + \{(CH_3)_3CFe^{III}Cl_2\}$$

The product dichloride undergoes decomposition via β-hydrogen elimination. An intermediary iron dichlorohydride is formed alongside 2-methylpropene:

$$\{(CH_3)_3CFe^{III}Cl_2\} \rightarrow (CH_3)_2C{=}CH_2 + [HFe^{III}Cl_2]$$

The iron hydride is capable of reducing acetone:

$$[HFe^{III}Cl_2] + (CH_3)_2C{=}O \rightarrow [(CH_3)_2CHOFeCl_2]$$

$$[(CH_3)_2CHOFeCl_2] + MgCl_2 \rightarrow FeCl_3 + (CH_3)_2CHOMgCl$$

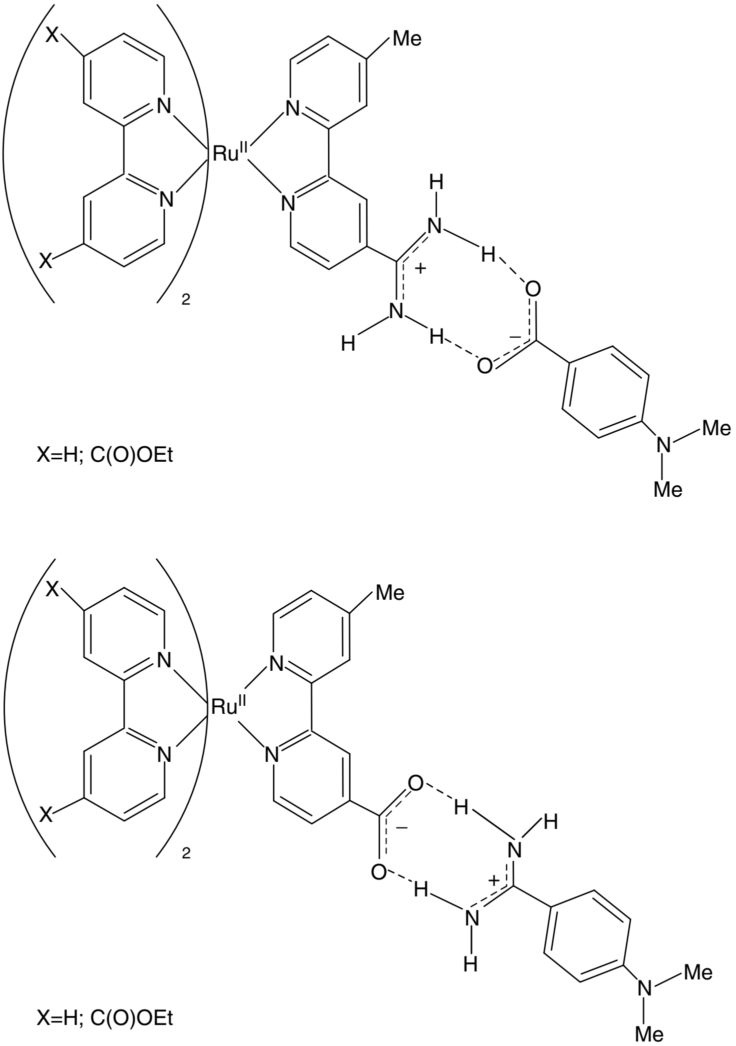
$$(CH_3)_2CHOMgCl + H_2O \rightarrow Mg(OH)Cl + (CH_3)_2CHOH$$

As shown earlier, *N*,*N*-dimethylaniline acts as an electron donor toward the electronically excited Ru(II) tris(dipyridyl)complex (Bock et al. 1979). Nocera's group studied the effect of salt formation on the redox interaction between the ruthenium complex and the *N*,*N*-dimethylaniline moiety. Two different salts, depicted in Scheme 5.26, were prepared and studied (Deng et al. 1997, Kirby et al. 1997, Roberts et al. 1997).

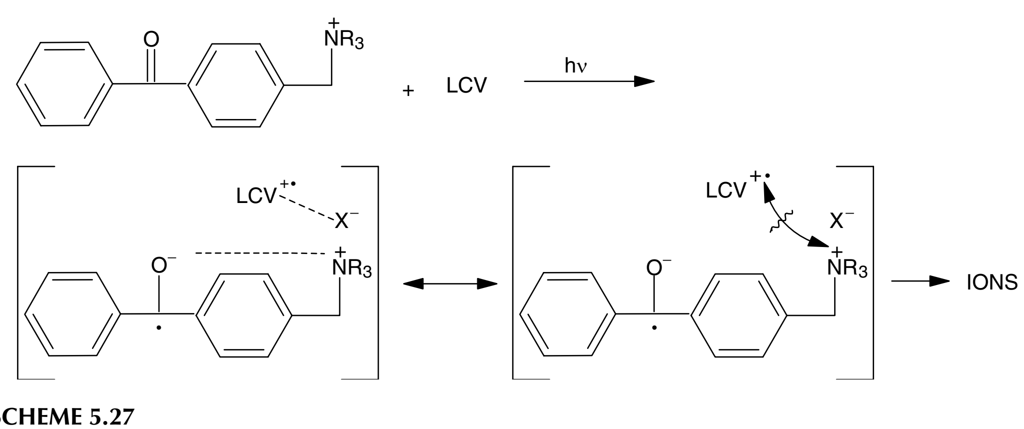
In the salts shown in Scheme 5.26, the amidinium-carboxylate hydrogen-bonded bridges are exceptionally stable. These bridges persist in solutions, even when the dielectric constant of the solvent is high. Such structures open up the possibility of considering the orientation of the salt bridge relative to the direction of electron transfer from the dimethylaniline donor to the metallocomplex acceptor. The rate of electron transfer along the donor–[carboxylate → amidinium]–acceptor route is significantly higher than that along the route when the interface is switched, that is, for the case of donor–[amidinium → carboxylate]–acceptor. In the carboxylate-amidinium orientation, the electron transfer obeys the direction of the permanent dipole of the salt bridge. However, when the cationic component is incorporated in the donor molecule, and the anionic component becomes incorporated in the acceptor counterpart, the salt bridge still works although such an arrangement is less favorable. Accordingly, the rate of electron transfer from the *N*,*N*-dimethylaniline moiety to the ruthenium complex is diminished.

Incorporation of an ionic component into a donor/acceptor molecule is also a very effective way of suppressing back electron transfer. One interesting example consists of the photooxidation of the leuco crystal violet (LCV, the leuco base) to crystal violet (CV, the dye) by benzophenone bearing a quaternary ammonium ion (Tazuke and Kitamura 1984). In this case, the cation-radical of LCV formed is repulsed by the ammonium positive charge. At the same time, the benzophenone anion-radical remains stabilized by the attached cationic fragment (see Scheme 5.27). As shown in Scheme 5.27, two favorable results are achieved: The stabilization of an IRP by counterion exchange and the charge separation by coulombic repulsion between the two positive charges. This leads to 100% efficiency of the photooxidation. With unsubstituted benzophenone itself, the efficiency does not exceed 20%. In the absence of $-NR_3^+X^-$ group in benzophenone, the efficiency remains small.

Photoinduced electron-transfer rates can be considerably reduced when X^- changes from chloride to bromide. Charge transfer between the cationic part of a molecule and the bromide ion may be



SCHEME 5.26



SCHEME 5.27

responsible for the rate reduction of photoinduced electron-transfer rates. Such a counterion effect on the photoinduced electron transfer and the reverse process has been demonstrated as examples of porphyrin-viologen linked compounds (Mitsui et al. 1989).

5.6 CONCLUSION

This chapter discussed the methods of regulating ion-radical transformations with respect to the nature of reacting species. These species possess both an ionic and a radical character at the same time. Being charged, the species demand a specific selection of solvents and salt additives and obey laws on ion-pair behavior. Species having an unpaired electron are susceptible to magnetic effects, sometimes to light, microwave, or ultrasound irradiation, and are especially sensitive to factors of spin density distribution. Coexistence of these ionic and radical properties defines a rather wide set of methods for suppressing undesirable processes or for stimulating reactions leading to the required final products.

Meanwhile, ion-radicals differ from ions and neutral molecules in their lower stability. As a rule, ion-radicals exist at lower temperatures. Therefore, heating is not a typical way to stimulate ion-radical reactions. Such reactions often require a controlled (inert) atmosphere, apparatus with polished walls, and so on. In general, approaches to the stimulation of ion-radical reactions do not seem to be quite regular or usual for organic chemists. Nevertheless, the high activity of ion-radicals permits different kinds of directed influence over the reactions, which follow ion-radical mechanisms.

The two questions are inseparable: How to optimize ion-radical reactions and how to facilitate electron transfer? As it has been noted in preceding chapters, electron transfers between donors and acceptors can proceed as outer- or inner-sphere processes. In this connection, the routes to distinguish and regulate each process should be mentioned. The brief statement by Hubig et al. (1999) seems to be appropriate: Outer-sphere electron transfers are characterized by (1) bimolecular rate constants that are temperature dependent and well correlated by Marcus theory, (2) no evidence for the formation of (discrete) encounter complexes, (3) high dependency on solvent polarity, and (4) enhanced sensitivity to kinetic-salt effects. Inner-sphere electron transfers are characterized by (1) temperature-independent rate constant that are greatly higher and rather poorly correlated by Marcus theory, (2) weak dependency on solvent polarity, and (3) low sensitivity to kinetic salt effects. This type of electron transfer does not produce ion-radicals as observable species but deals with the preequilibrium formation of encounter complexes with the charge-transfer (inner-sphere) nature (see also Rosokha and Kochi 2001).

One important feature of ion-radical organic reactions consists of a possibility to nudge them by the introduction of active reactants. Thus, in the reaction of an electron acceptor with electron donors (nucleophiles), the addition of a tiny amount of a nucleophile, which is more active at initiation of the one-electron transfer allows the less reactive nucleophile to start its own chain propagation. A method called “entrainment” is widely used in chemical practice; as a recent example (see Schmidt et al. 2007).

The choice of the right solvent is an everyday decision for the chemist: Which solvent would be the best to dissolve certain products, and what solvent would lead to increased reaction yields or rates of the reaction? As applied to the electron-transfer reactions and the reactions of the ion-radical formed, these questions seem to be less perplexing for the readers by means of considerations mentioned in Section 5.4.

Presently, efforts are oriented to friendly ecology of chemical processes. Sometimes, changes of organic solvent media to water or usage of ionic liquids seems to be possible. A series of ion-radical reactions are exemplified here and in Chapter 2. Mechanic activation opens a possibility to perform chemical transformations without solvents at all. Some mechanoinduced ion-radical organic reactions from Section 5.2.6 are incentive in this sense, too.

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6 Stereochemical Aspects of Ion-Radical Organic Reactions

6.1 INTRODUCTION

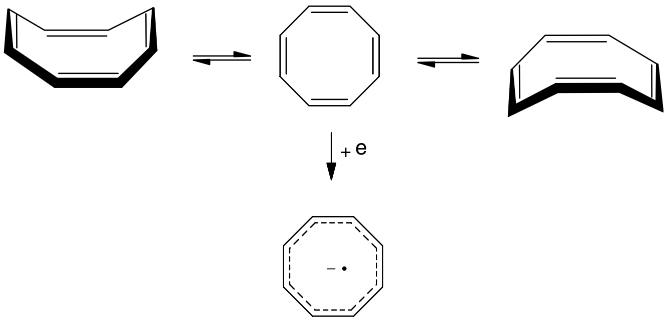
Although organic ion-radicals differ from their corresponding parent (uncharged) molecules only by one electron, this difference can lead to large modifications not only in terms of their chemical reactivity but also to fundamental stereochemical changes. Several reviews have focused on this feature of ion-radical organic chemistry (Todres 1974, Pedulli 1993). The electron transfer obeys the Franck–Condon principle and takes place within such a short time that there is no nuclear motion. However, many organic compounds can oscillate between diverse conformational isomers, and one-electron transfer can trigger one of them. Only those isomers that are the most favorable for the existence of an unpaired electron on the corresponding somomer can be triggered. Somomers are electromers differing in their SOMO. Thus, the tube conformation is the most stable for cyclooctatetraene. The tube conformer can exist as a bath standing normally or as a bath turned over. The flat cyclooctatetraene definitely exists between the normal and turned conformers. The cyclooctatetraene anion-radical is a planar or an almost planar species. The planar, 9-π electron anion-radical structure of cyclooctatetraene is closer to the aromatic (planar and stabilized) structure of the dianion with $4n + 2 = 10$-π electrons than that of the parent neutral molecule. This is the reason why one-electron transfer is able to trigger the intermediary flat conformation of cyclooctatetraene (Scheme 6.1). Naor and Luz (1982) made a stand for this point of view. This feature agrees with the Franck–Condon principle and with the thermodynamic demand of similarity between structures of the transition state and the product.

At the same time, it is possible that one-electron transfer creates conditions favorable for the existence of a definite conformer, which leads to corresponding stereochemical consequences.

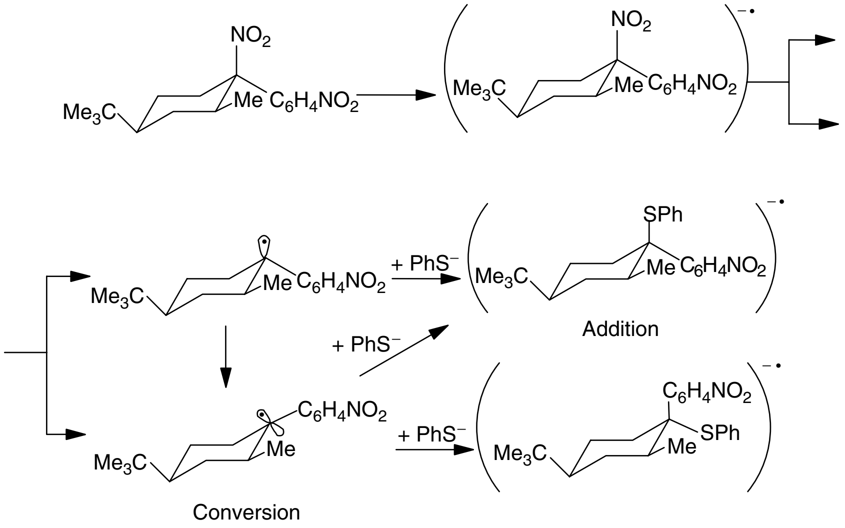
6.2 PROBLEM OF STERIC RESTRICTIONS

In ion-radical organic chemistry, the problem of steric restrictions has many aspects. The main aspect concerns typical stereochemical consequences of electron transfer such as changes in bond distance, bond and torsion angles, as well as renewed conditions of spin (charge) distribution within the molecular skeleton. For instance, propensity of sterically crowded bicyclo[1.1.0]butanes to rearrange into cyclobutane derivatives is diminished after one-electron oxidation. As shown by Saettel and Wiest (2003), this process results in the lengthening of the bond that is common for the two cyclopropane rings. Because each cyclopropane ring can delocalize the spin–charge density, the cation-radical formed differs with enhanced stabilizing delocalization. The presence of substituents (even the bulky *tert*-butyl groups) creates a strong steric hindrance. Nevertheless, such an effect is not sufficient to overcome the effects of bond elongation and additional electron-charge delocalization.

Ion-radical organic reactions of the $S_{RN}1$ type are less sterically restricted than classical S_N reactions. Generally, the nucleophilic (not S_{RN}) reactivity varies with the steric demand at the reaction center. The electron-transfer reactivity does not depend on steric effects. To illustrate this, one can compare electron transfer and nucleophilic reactivity between ketene silyl acetals and cationic electrophiles (Fukuzumi et al. 2001). Nevertheless, space strains may determine the overall results of these reactions if either intermediate radicals or forming products are sterically hindered.



SCHEME 6.1

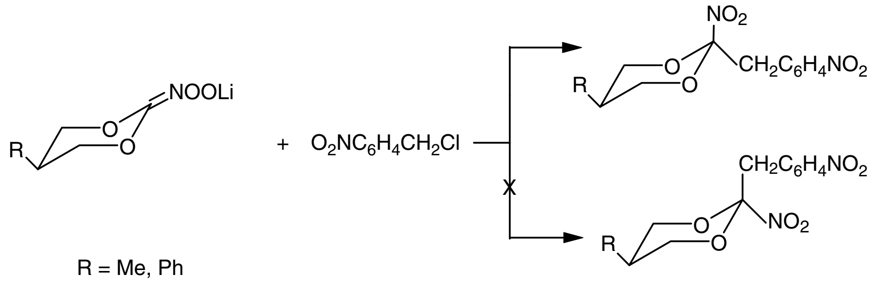


SCHEME 6.2

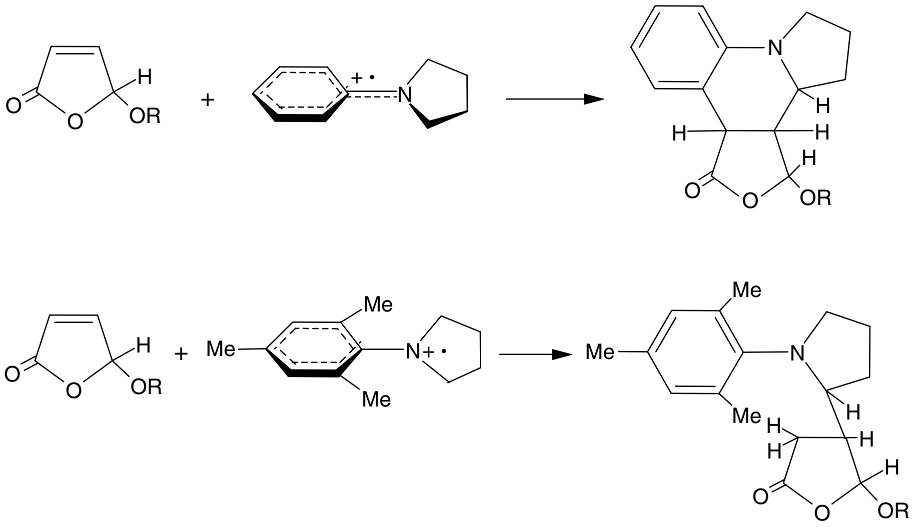
Scheme 6.2 shows the case in which the *intermediate radical is sterically hindered*, whereas the reactant is strongly active with respect to the radical (Norris and Smyth-King 1982).

Scheme 6.2 represents $S_{RN}1$ substitution that takes place when sodium thiophenolate attacks *e*,4-*tert*-butyl-*e*,2-methyl-*a*,4-nitro-*e*,4-(4-nitrophenyl) cyclohexane. Light irradiation stimulates the reaction. It is carried out under nitrogen in HMPA. The ion-radical type of the process has been established by means of inhibitors. It was found that the stereochemical outcome of the reaction depends on the concentration of the PhSNa nucleophile. At a low concentration of PhSNa, the reaction leads to a mixture of phenylthiyl derivatives; the content of *a*,SPh-substituted product is higher than that of *e*,SPh product by 20%. At a high concentration of PhSNa, the reaction produces practically a single stereoisomer bearing the *a*-PhS group.

In the course of the reaction, the nitrite ion leaves the primary anion-radical. This produces the cyclohexyl radical in the pyramidal configuration. The vicinal methyl group sterically hinders the conversion of the pyramidal radical into the planar one. With a high concentration of the nucleophile, the rate of addition exceeds the rate of conversion, that is, $r_{add} > r_{conv}$. Then the entering PhS group occupies the axial position. With a low concentration of the nucleophile, the conversion occurs earlier than the addition ($r_{add} << r_{conv}$) and the planar radical center is attacked from both axial and equatorial sides. This results in the formation of an isomer mixture. Certainly, the simultaneous



SCHEME 6.3



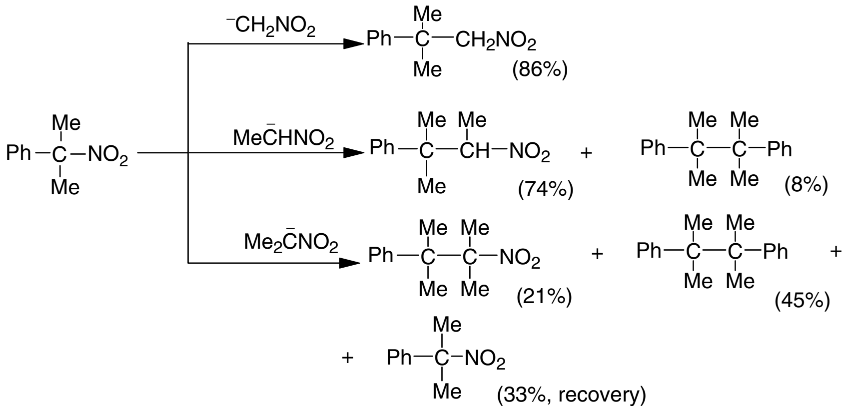
SCHEME 6.4

formation of planar and pyramidal radicals and their mutual interconversions are possible. Nevertheless, the explanation of the stereospecificity given earlier seems sufficient.

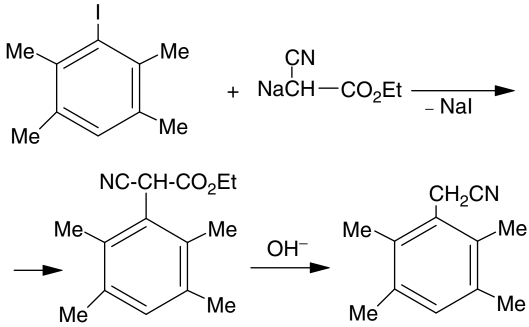
The stereospecific substitution produces a sterically less strained product when a more bulky *p*-nitrophenyl substituent occupies the equatorial position and the less bulky phenylthiyl substituent occupies the axial position. Steric limitations of the nucleophile attack caused by *strains in the final product* are thus removed. And therefore, ion-radical addition of *p*-nitrobenzyl radical to the lithium salts of 5-nitro-1,3-dioxanes proceeds stereospecifically (Zorin et al. 1983; Scheme 6.3).

Steric encumbrance *in the attacking reactant* blocks the $S_{RN}1$ reaction by a standard manner (Look and Norris 1999). If the attacking reactant protrudes in the ion-radical form, the reaction results depend on the manner of spin–charge distribution within this form. Thus, *N*-phenylpyrrolidine cation-radical forms a nitrogen-containing heterocycle as a result of cycloaddition to menthoxyfuranone, whereas the *N*-mesitylpyrrolidine cation-radical is unable to form the cyclic product; compare courses of the two photoreactions shown in Scheme 6.4 (Griesbeck et al. 2007).

The difference in reactivity depicted in Scheme 6.4 is certainly linked to the enrichment of the phenyl ring in the *N*-phenylpyrrolidine cation-radical with spin density. The mesityl fragment in *N*-mesitylpyrrolidine is brought out of the spin distribution being located in the orthogonal plane with respect to the nitrogen-containing moiety. Thus, only the nitrogen-centered ring takes part in the reaction.



SCHEME 6.5



SCHEME 6.6

Let us follow the role of *steric hindrance in a forming product* during the course of $S_{RN}1$ process according to Kornblum and Erickson (1981) as well as Akbulut et al. (1982). Scheme 6.5 clearly demonstrates the effect; here, all of the constituent reactions were performed in equal conditions (HMPA as a solvent, at 25°C). The $S_{RN}1$ nature was proven for all the cases. The intermediary cumyl radical reacts with the nitroalkane anion, but this reaction is retarded with an increase in the size of an alkyl anion. The significance of the cumyl radical dimerization grows accordingly.

Compared to classical substitutions, $S_{RN}1$ reactions are, in general, not so strongly dependent on steric factors. This feature is employed for synthetic purposes. For instance, the cyanoacetate substituent was inserted in the sterically shielded position of a benzene ring (Suzuki et al. 1983; Scheme 6.6).

The reaction shown in Scheme 6.6 takes place in HMPA. Photoirradiation results in the formation of undesirable by-products, but the initiation with cuprous iodide leads to the aimed substance with more than 60% yield.

Dimerization of arylamine cation-radicals is a prominent example of the product's steric hindrance effects on the reaction course. Although stable in AN, the *N,N*-dimethyl-*p*-toluidine dimerizes if its uncharged counterpart is present in the solution (Goto et al. 2002, Oyama and Goto 2003). The cation-radical loses a proton, and the parent amine reacts as a base, accepting this proton. Coupling of benzylic radicals is an understandable result of the following reaction:

$$[p\text{-}(CH_3)_2NC_6H_4CH_3]^{+\bullet} \rightarrow H^{+\bullet} + p\text{-}(CH_3)_2NC_6H_4CH_2^{(\bullet)}$$

$$\rightarrow p\text{-}(CH_3)_2NC_6H_4CH_2 - CH_2C_6H_4N(CH_3)_2\text{-}p'$$

The reaction course principally changes as a result of CH_3 relocation from the para to ortho position of the benzene ring. Because of steric hindrance at the benzylic radical center, the dimerization is directed to the free para position of the benzene ring and the corresponding benzidine occurred as the final product (Oyama and Kirihara 2004).

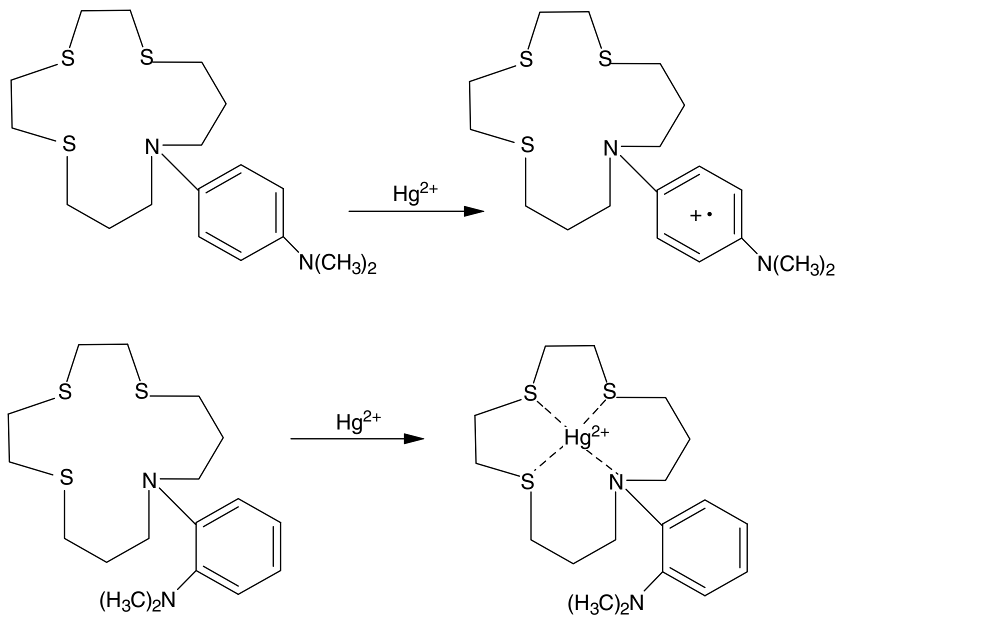
$$[o\text{-}(CH_3)_2NC_6H_4CH_3]^{+\bullet} \rightarrow H^+ + o\text{-}(CH_3)_2NC_6H_4\ CH_2^{(\bullet)} \leftrightarrow o\text{-}(CH_3)_2NC_6H_3^{(\bullet)}CH_3$$

$$o\text{-}(CH_3)_2NC_6H_3^{(\bullet)}CH_3 \rightarrow o\text{-}(CH_3)_2N(CH_3)C_6H_3\text{–}C_6H_3(CH_3)N(CH_3)_2\text{-}o'$$

Another important aspect of steric restriction concerns the difference in internal energies between neutral and ion-radical states of a molecule. Thus, in its neutral state, *cis*-1,3,5-hexatriene is free to adopt three conformers (cis—cis—cis, cis—cis—trans, and trans—cis—trans) by rotation around a single bond with a barrier of only 4 kJ · mol^{-1}. For the cation-radical state, this barrier height increases up to 46 kJ · mol^{-1}, thus making the interconversion of the conformers a slow process compared to that of the neutral molecule. The trans—cis—trans conformer of the cation-radical possesses the lowest internal energy. Being involved in the cation-radical state, 1,3,5-hexatriene does not undergo ring closure. The origin of such inertness is the rapid formation of the trans—cis—trans conformer, where the carbon termini are too far away from each other to close the possible six-membered ring (Radosevich and Wiest 2001).

A striking example of the steric restriction considered is given by Sibert et al. (2006). This example concerns the reaction of mercury(2+) with para or ortho isomer of Wuerster azathiacrown ether. Although the para isomer transforms into the analog of Wuerster blue (into the cation-radical), the ortho isomer acts as a host for the mercury cation, giving rise to the inclusion complex (Scheme 6.7).

The authors explain the difference through the ortho effect that hinders *o*-Wuester azathiacrown ether from one-electron oxidation but assists in the mercury coordination inside the macrocycle (Sibert et al. 2006).



SCHEME 6.7

6.3 REFLECTION OF THE ION-RADICAL STEP IN REACTION STERIC RESULTS

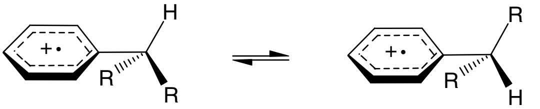
It can now be reminded that deprotonation of a cation-radical is subject to stereoelectronic control. The C—H bond has to align with the SOMO of the cation-radical's preferential conformation for the C—H bond cleavage. When this conformation cannot be reached, the deprotonation rate slows down significantly. To reach the needed alignment, energy has to be utilized. In the case of alkylaromatic cation-radicals, the preferential conformation for the cleavage is orthogonal C—H bond disposition with respect to the plane of the aromatic ring (Baciocchi et al. 2006; Scheme 6.8).

For works concerning nucleophilic substitution refer de Lijser et al. (2001) and references therein. The authors dealt with cis and trans isomers of 1,3-dimethyl-1-(4-methoxybenzyl)sylacyclobutane and compared their reactions with methanol for cases where the substrates exist in their neutral or cation-radical forms. In all the cases, 1,3-dimethyl-1-methoxysilacyclobutanes were obtained. In neutral silacyclobutanes, the substitution proceeds with the retention of configuration at silicon. On the contrary, the cation-radical substitution occurs with inversion (Scheme 6.9). The reaction rates were higher for the neutral substrates than for the cation-radicals. Substitution in neutral silacyclobutanes seemingly proceeds by a stepwise mechanism. This rationalizes the retention of stereochemistry. The higher reaction rates can be explained by the release of bond angle strain during the formation of the pentacoordinative intermediate. The inversion mechanism depicted in Scheme 6.9 explains the observed diminution of the reaction rates. This is a concerted mechanism where no preliminary strain release takes place, but the methoxyl addition and departure of the leaving group proceeds at the same time. Such a process requires more energy. The rates of these cation-radical reactions understandably decrease.

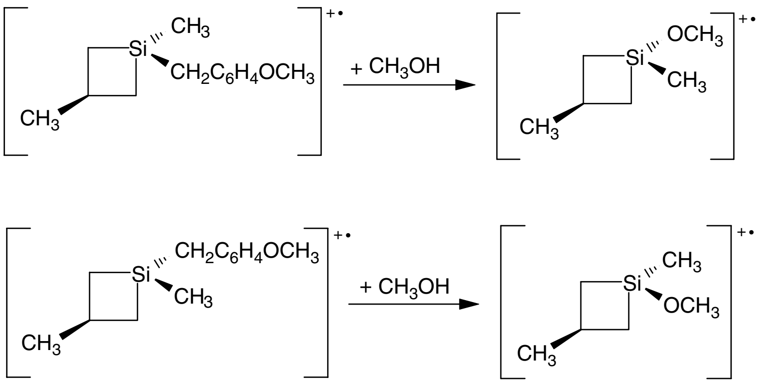
The chiral nucleophiles $C_6H_{13}C^*H(Me)X$ (X = Br, OSO_2Me) alkylate the benzophenone metal ketyl at one of the rings as well as at the carbonyl carbon atom. Both pathways lead to the corresponding products in approximately equal amounts (Hebert et al. 1983; Scheme 6.10).

The ketone is formed as a racemate (with respect to the alkyl substituent). Consequently, the main route includes an electron-transfer step (see Scheme 6.11).

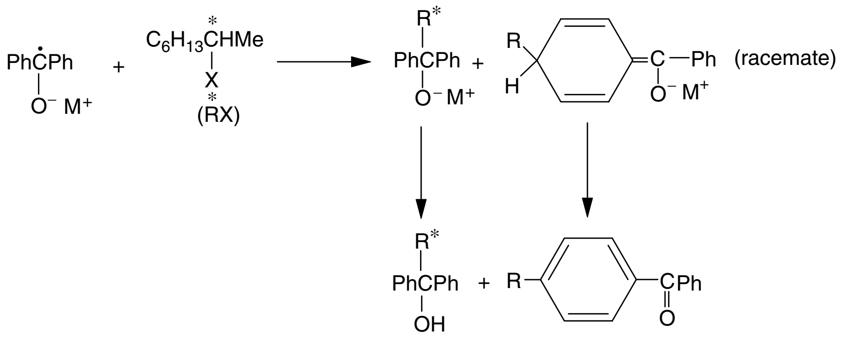
Let us return to Scheme 6.10 and consider the fate of the diphenylalkyl carbinol formed. The carbinol is optically active, and a configuration inversion takes place partially. Obviously, a dual reactivity is observed. Accordingly, the electron-transfer route can be represented by Scheme 6.12.



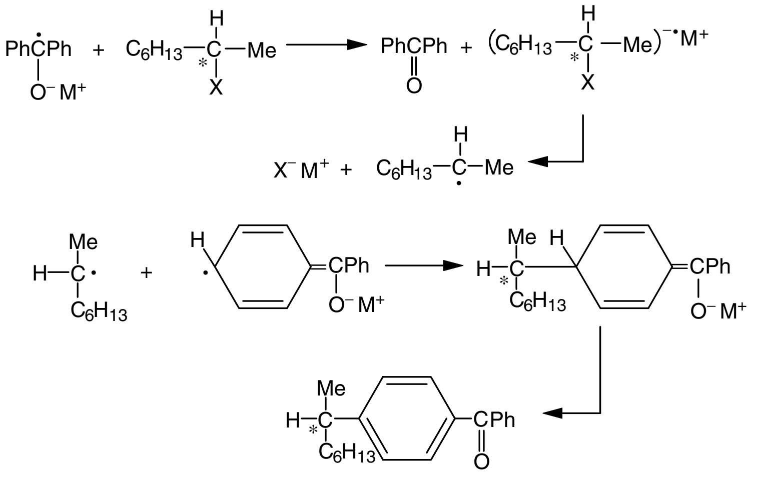
SCHEME 6.8



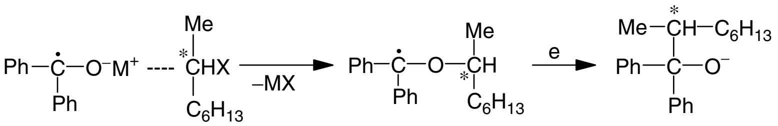
SCHEME 6.9



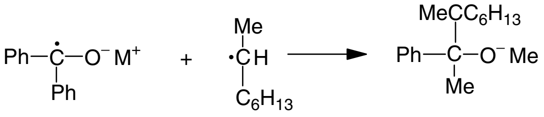
SCHEME 6.10



SCHEME 6.11

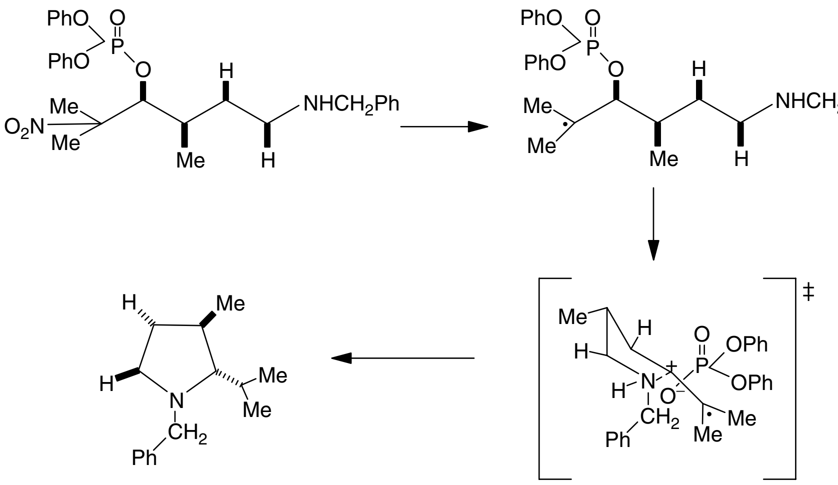


SCHEME 6.12



SCHEME 6.13

As emphasized by Bakken et al. (2001), the observation of an excess of inversion of the configuration in the C–C alkylated products obtained by the reaction in Scheme 6.12 may well be the result of a single transition state that gets divided into the electron-transfer product and substitution product. In fact, the amount of enantiomeric excess in such a reaction can serve as a measure of the bonding in the electron-transfer transition state. Scheme 6.13 depicts the S_N2 route.



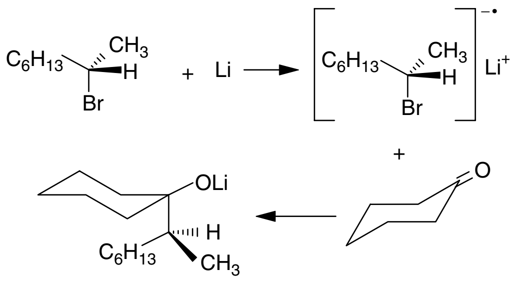
SCHEME 6.14

The nature of X in the initial $C_6H_{13}C^*H(Me)X$ defines the relation between the two routes. If X = Br, the configuration inversion does not exceed 8%. If X = OSO_2Me, the inversion takes place up to 25%. The bromide ion is more active in elimination than methyl sulfonate ion. Therefore, the electron-transfer contribution to the substitution reaction is higher.

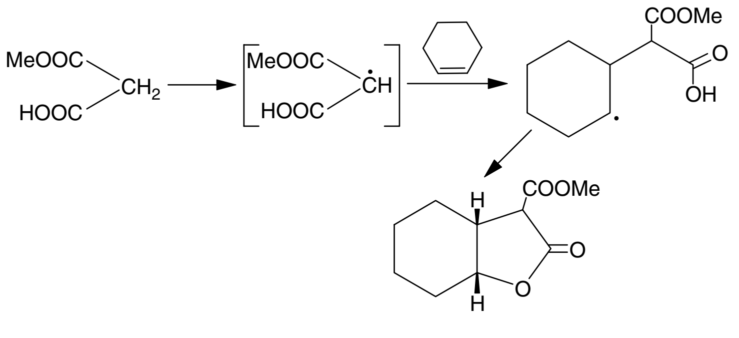
In Section 2.2.2, the reductive way to cation-radicals was discussed, which consists of the initial removal of a function of good fugacity from α,β-functionalized alkanes (Crich et al. 2006). This initial removal generates a radical center at the α position. Appearance of the radical center assists in the elimination of another function of lower fugacity from the β position (α effect). When such a reaction proceeds with an alkane bearing the α-nitro and β-phosphatoxy groups, an interesting diastereoselective intermolecular cyclization takes place (Crich and Ranganathan 2005). Scheme 6.14 demonstrates stereoselectivity of the reaction. The cyclization takes place at the level of the initial contact ion pair with the attack by the amine of the opposite face of the cation-radical to the one shielded by the just-departed phosphate group. The cyclization proceeds rapidly before any conformational transition is finished. This makes the peculiar effect of stereochemical memory possible. This approach is actively used in diastereoselective synthesis, and yields are high enough (see, e.g., Sartillo-Piscil et al. 2003).

The alkylation of ketones by haloalkyls in the presence of alkali metals is known as the Barbier reaction. Luche and Cintas (1999) compared the stereochemical results of the reaction with the participation of cycohexanone, homochiral 2-bromooctane, and lithium metal under the typical conditions of Barbier reaction (at 0°C, stirring) or on ultrasonic stimulation (at −50°C). As noted in Section 5.2.5, rate-determining electron-transfer steps are dependent on the sonication effect. From $C_6H_{13}C^*H(Me)Br$, the reactive entity is the anion-radical generated on the activated metal surface. Under sonication conditions, the reaction is completed in 1.5 h and leads to 98% yield of the product. The latter is formed in a partially inverted configuration. The inversion degree is 19% at a medium-energy sonication and increases up to 24% for high-energy sonication. Under the conditions of Barbier reaction, the yield barely reaches 50% for 7 h, and the degree of configurational inversion does not exceed 6%. According to Luche and Cintas (1999), sonication increases the concentration of the primary haloalkane anion-radical and accelerates its addition to the carbonyl group, in a direction anti to the leaving bromide ion. The conventional reaction (without sonication) provides much lower yields of a practically racemic product. The overall sonicated reaction proceeds as shown in Scheme 6.15.

It should be noted that nonmetallic redox reactions also experience the sonication influence. The preparation of γ lactons from olefines by oxidation of manganese triacetate is an example.



SCHEME 6.15



SCHEME 6.16

The reaction with monomethyl malonate in acetic acid, which does not occur at 0–10°C, proceeds smoothly when sonication is applied (Allegretti et al. 1993). From cyclohexene, only the cis ring fusion in bicyclic lactone is observed; the product is formed at 80% yield for 15 min at 10°C. The overall transformation, in brief, is shown in Scheme 6.16. The stereoselectivity of the sonochemical process probably reflects the enhanced reaction rate, which does not allow equilibration processes to take place.

6.4 CONFORMATIONAL TRANSITION OF ION-RADICALS

This problem has attracted considerable attention, and intriguing results have been obtained. It would be important, however, to develop some applications in organic photodiodes, transistors, sensors, and charge-storage devices.

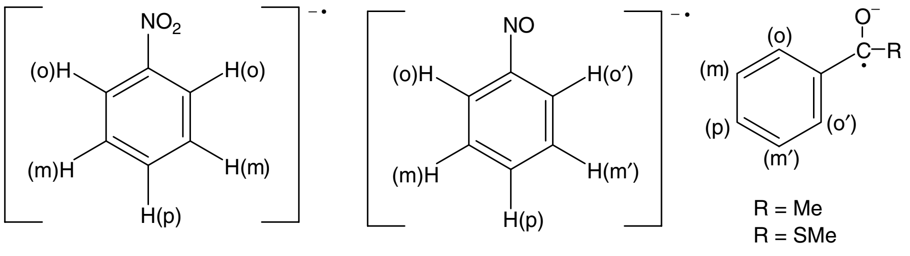
For instance, poly-*p*-phenylenes in their doped states manifest high electric conductivity (Shacklette et al. 1980). Banerjee et al. (2007) isolated the hexachloroantimonate of 4‴-di(*tert*-butyl)-*p*-quaterphenyl cation-radical and studied its x-ray crystal structure. In this cation-radical, 0.8 part of spin density falls to the share of the two central phenyl rings, whereas the two terminal phenyl rings bear only 0.2 part of spin density. Consequently, there is some quinoidal stabilization of the cationic charge or polaron, which is responsible for the high conductivity. As it follows from the theoretical consideration by Bredas et al. (1982), the electronic structure of a lithium-doped quaterphenyl anion-radical also differs in a similar quinoidal distortion. With respect to conformational transition, this means less freedom for rotation of the rings in the ion-radicals of quaterphenyl. This effect was also observed for poly-*p*-phenylene cation-radical (Sun et al. 2007) and anion-radical of quaterphenyl *p*-quinone whose C—O bonds were screened by *o*,*o*-*tert*-butyl groups (Nelsen et al. 2007).

In this sense, binaphthyls are of interest due to the great conformational difference between the corresponding neutral molecules and ion-radicals. The most stable conformation of 1,1′-binaphthyl is that in which the naphthalene rings form an angle of 70°. This leads to a very small π overlap and the existence of two enantiomers (atropoisomers) differing in the arrangement of one naphthyl moiety above or below the plane of the other. This torsion angle is diminished to approximately 50° in the anion-radical form so that the unpaired electron acquires the possibility to delocalize over the whole binapthyl molecule, with the loss of chirality (Eisenstein et al. 1977, Baumgarten et al. 1993). The same situation arises when 1,1′-binaphthyl-4,4′-diamine is transformed into the cation-radical. Naturally, this cation-radical belongs to the ammoniumyl class. The naphthyl–naphthyl torsion angle is diminished up to 55° and the unpaired electron is effectively delocalized between the singly oxidized and neutral naphthalene amine moieties. This is for the cation-radical. The two-electron oxidation leads to the dication-diradical of 1,1′-binaphthyl-4,4′-diamine. In the dication-diradical species, the torsion angle is restored and two ammoniumyl moieties exist independently. Electrochemical, UV or ESR spectral, magnetic, and energy properties were found to be different for the neutral, cation-radical, and dication-diradical forms of *N*,*N*′-disubstituted 1,1′-binaphthyl-4,4′-diamine (Desmarets et al. 2006).

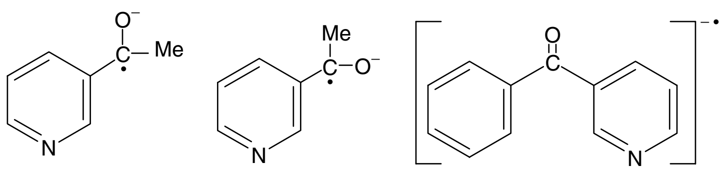
Buta-1,3-diene has *s*-trans-planar structure (Aston et al. 1946). Its perfluoro derivative, 1,1,2,3,4,4-hexafluorobuta-1,3-diene (HFBD), is nonplanar with mutual cis orientation of the two ethylene fragments with respect to the central ordinary bond (Chang et al. 1971). This indicates that fluorine substitution has a significant effect on the molecular and electronic structures of butadiene. However, when HFBD loses one electron to form the cation-radical, its structure becomes planar irrespective trans or cis conformation had the parent diene (Xiao et al. 2007). Apparently, both the ethylene bonds participate in the formation of SOMO and this allows overcoming of the not so strong steric hindrance occurring as a result of fluorine substitution.

The anion-radicals from aromatic nitro compounds preserve the second-order axis of symmetry. The analysis of superfine structure of the ESR spectrum of the nitrobenzene anion-radical reveals equivalency of the ortho and meta protons (Ludwig et al. 1964, Levy and Myers 1965). With the anion-radical of nitrosobenzene, the situation is quite different. This was evidenced from the ESR data (Levy and Myers 1965, Geels et al. 1965). Following electron transfer, the bent nitroso group fixes in the plane of the benzene ring to a certain extent. This produces five different types of protons, since both meta and ortho protons become nonequivalent. The nonequivalence of the ortho and meta protons has also been established for the anion-radicals of acetophenone (Dehl and Fraenkel 1963) and *S*-methylthiobenzoate (Debacher et al. 1982; Scheme 6.17).

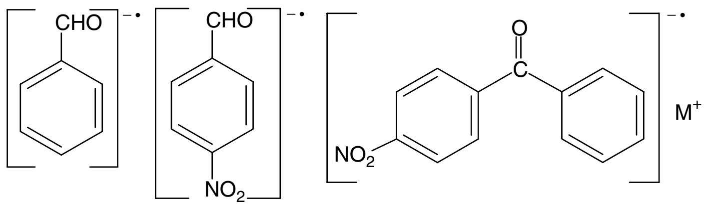
During transformation from the neutral molecules to the corresponding anion-radicals, the rate of the fragment rotation, relative to one another, decreases. This also results in the nonequivalence of the meta and ortho protons. Thus, 3-acetylpyridine gives two different anion-radicals as conformational isomers (Cottrell and Rieger 1967). In the case of 3-benzoylpyridine anion-radical, the phenyl group rotates freely about the carbonyl center, whereas the rotation of the pyridyl group is limited. The ESR spectrum shows that the spin density in the phenyl ortho positions is half of that



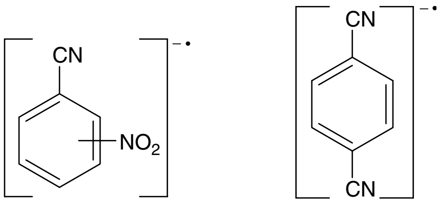
SCHEME 6.17



SCHEME 6.18



SCHEME 6.19



SCHEME 6.20

in the pyridyl ortho position (Sevenster and Tabner 1981). Therefore, the pyridyl fragment interacts with the negatively charged carbonyl oxygen stronger than the phenyl. The strong interaction fixes the pyridyl moiety and increases the barrier of its rotation about the ketyl center (Scheme 6.18).

As a rule, if the unpaired electron density in the anion-radical is redistributed, the rotation barrier decreases. Thus, the barrier of the phenyl rotation in the benzaldehyde anion-radical is equal to 92 kJ · mol^{-1}, whereas in the 4-nitrobenzaldehyde anion-radical, the barrier decreases to 35 kJ · mol^{-1} (Branca and Gamba 1983). Ion-pair formation enforces the reflux of the unpaired electron from the carbonyl center to the nitro group. Being enriched with spin density, the nitro group coordinates the alkali metal cation and fixes the unpaired electron to a greater degree. The electron moves away from the rotation center. The rotation barrier decreases. The effect was revealed for the anion-radical of 4-nitrobenzophenone and its ionic pairs with lithium, sodium, potassium, and cesium (Branca and Gamba 1983; Scheme 6.19).

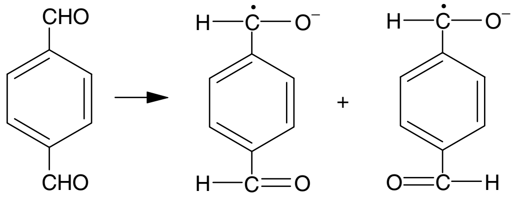
Surprisingly, the anion-radicals of isomeric nitrobenzonitriles (Scheme 6.20) keep the equivalency of the ring in the two ortho positions around the cyano group (Subramanian et al. 1972). This does not mean that the cyano group attracts the unpaired electron stronger than the ketyl group. The reason lies rather in the linearity of the cyano group and its location along the ring symmetry axis. As demonstrated by Nakamura 1967, in the anion-radicals of *p*-dicyanobenzene the cyano groups and all the unsubstituted four-ring protons are equivalent. This equivalency was also corroborated with experimental IR and theoretical comparison between *p*-dicyanobenzene and its anion-radical (Stambolliyska 2005).

Benzene *p*-dialdehyde (terephthalic aldehyde) produces the anion-radical at the potential of the limiting current of its first reduction wave in DMSO with tetrapropylammonium salt as a supporting electrolyte. The anion-radicals demonstrate two ESR spectra. One of them is superimposed

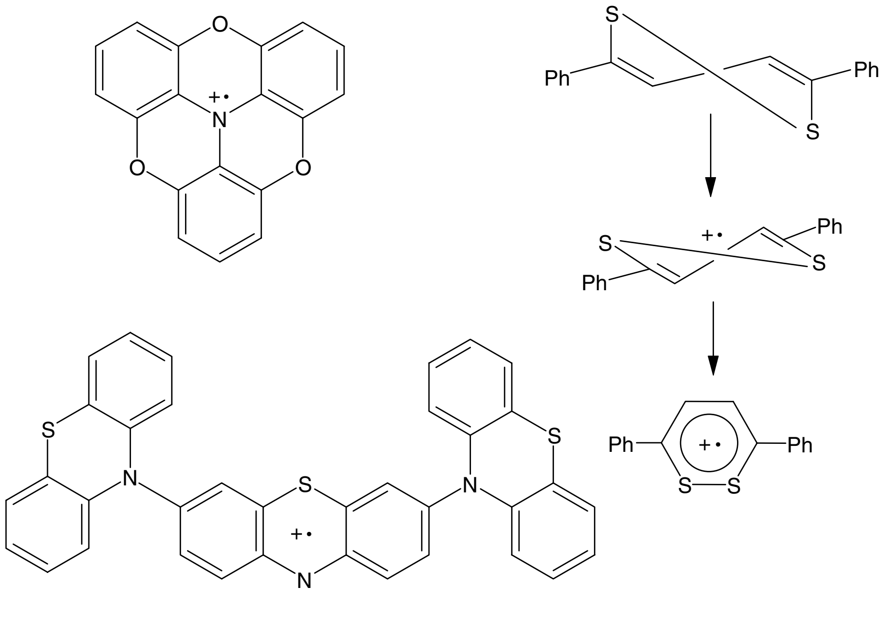
over the other. They have the same *g*-factor but considerably differ in the splitting constants (Stone and Maki 1963). If the rate of rotation of the aldehyde groups were many times greater than the frequency difference in the splitting constants of cis and trans rotamers, the ESR spectra of the anion-radicals of terephthalic aldehyde would be averaged. If the rate of mutual rotation of the groups were comparable with the difference in the splitting constants of the rotamers, the lines of the spectra would widen. The spectra overlap one another; this means that the frequency of rotation is much lower than the frequency difference in splitting constants. It seems improbable that the formation of different (contact, separated) ionic pairs of one and the same anion-radical with the countercation is responsible for such a superposition of spectra—tetraalkylammonium was used as the cation, and this cation practically does not form arbitrarily stable ionic pairs. According to calculations (Nelsen et al. 2005), the trans anion-radical of terephthaldehyde is more stable than the cis anion-radical by 0.88 kJ · mol^{-1}. The analysis of the ESR line intensities reveals that the cis and trans forms of this anion-radical are in the ratio 1:1.4 (Stone and Maki 1963). Hence, electron transfer to terephthalic aldehyde yields two conformers as depicted in Scheme 6.21.

Let us consider chalcogen-containing ion-radicals. Scheme 6.22 represents three typical cases.

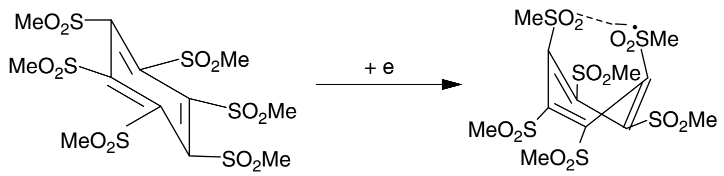
The oxygen-bridged triphenylamine (2,2′:6′,2″:6″,6-trioxatriphenylamine) has a shallow-bowl structure. The corresponding cation-radical acquires a practically planar structure. This cation-radical is very stable, neither dimerization tendency in the crystalline form nor oxygenation



SCHEME 6.21



SCHEME 6.22



SCHEME 6.23

under aerated conditions in solution was observed (Kuratsu et al. 2005). The spin delocalization in the whole framework involves the oxygen atoms by the same manner as in 10-phenylphenoxazine cation-radical.

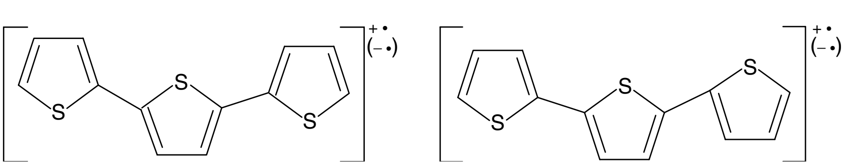
Henning et al. (2006) used spectroelectrochemical and DFT methods to follow conformational transition of 3,6-diphenyl-1,2-dithiin by one-electron oxidation. The primary cation-radical is flattened partially. This cation-radical was fixed at 223 K. Heating up to 293 K provided this cation-radical with an additional energy. It resulted in the formation of an entirely planar structure with complete spin delocalization within the molecular framework. The transition is depicted in Scheme 6.22.

The cation-radical of phenothiazine trimer, also shown in Scheme 6.22, has a central phenotiazine fragment that is almost flat, whereas the outer two phenothiazines are bent forming butterfly structures. The parent neutral trimer consists of all the three phenothiazines adopting the butterfly forms (Okamoto et al. 2004). The trimer cation-radical undergoes remarkable conformational transition. Its spin and charge are localized mainly on the central (flatten) phenothiazine fragment. Analogous stereochemical features were revealed for an extended tetrathiafulvalene (9,10-bis(1,3-dithiolene-2-ylidene)-9,10-dihydroanthracene), its cation-radical, and dication with the help of electrochemistry, photoelectron spectroscopy, and DFT calculations (Gruhn et al. 2006a).

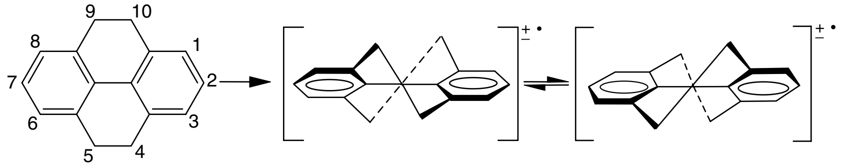
Neutral hexakis(methylsulfonyl)benzene (see Scheme 6.23) adopts a chair conformation. On the contrary, the tube conformer appears to be inherent in the corresponding anion-radical. The methylsulfonyl fragments at positions 1 and 4 of the bent benzene ring are nonequivalent. Moreover, one methylsulfonyl moiety is nonequivalent to all of the other five (Fabre et al. 2002). Scheme 6.23 depicts an intuitively constructed picture. Localization of spin–charge density within one methylsulfonyl group causes the attraction of the other from position 4. This makes the tube conformation the most stable in the case of hexakis(methylsulfonyl)benzene anion-radical.

As a rule, the transformation of a neutral molecule into an anion-radical results in the elongation of the multiple bonds and shortening of the ordinary bonds. Naturally, this can result in conformational changes. In the anion-radicals of 2,2′-bisthiazole (Pedulli et al. 1975) and 2,2′-bisbenzothiazole (Lopez-Calahorra et al. 2004), the partial double-bond character of the exocyclic ordinary bond connecting the two heterocyclic moieties causes the increase in the rotation barrier when compared to initial uncharged molecules. Accordingly, the ESR spectra revealed only one conformation, although two of them (*s*-trans and *s*-cis) can be expected. It should be noted, however, that the free rotation around C–C bond is hindered in the neutral bisthiazoles.

In contrast, 2,2′-bisthienyl ion-radicals is characterized with definite, although rather restricted, rotational freedom leading to the existence of *s*-trans and *s*-cis rotamers. According to ESR (Pedulli 1993) and Raman (Keszthelyi et al. 1999, 2000) spectra, the 2,2′-bithienyl anion-radical forms two rotational isomers. The 2,2′-bisthienyl cation-radical also exists as a mixture of at least two rotamers. No exchange broadening takes place even at temperatures as high as 100°C. The internal barrier is very high, approximately 70 kJ · mol^{-1}. Meanwhile, for 2,2′-bisthienyl (the neutral molecule), the magnitude of the rotation barrier is approximately 20 kJ · mol^{-1}. Restricted rotation was also observed both in anion and cation-radicals of terthiophene, that is, 2,5-bis(2-thienylo)thiophene, whose ESR spectra showed signals from two of the three possible conformational isomers up to



SCHEME 6.24



SCHEME 6.25

room temperature. The rotamers were formed as a mixture, containing the *s*-trans, trans- and *s*-cis, trans-forms (Pedulli 1993; Scheme 6.24).

The hexafluoroantimonate salt of the terthiophene cation-radical in which terminal thiophene was completely surrounded by bicycle[2.2.2] octane units was studied by x-ray crystallography (Nishinaga et al. 2004). In the crystal lattice, the authors did not find only one isomer. They wrote about the *dominant* form, which was an *s*-trans–trans conformer. The central thiophene ring remains free, and only the terminal rings are fused with the bicycle[2.2.2] octane units—this cation-radical acquires a bent conformation. As B3LYP calculations show, the all-anti conformer is more stable than the all-syn counterpart by 5.35 kJ · mol^{-1} (Yamazaki et al. 2006).

Alberti et al. (2003) considered spin delocalization in ion-radicals from tris(butylsulfonyl) sexithiophene in which all the thiophene rings are linearly bonded at the expense of the α positions. As it turned out, the unpaired electron in the cation-radical is mainly delocalized onto the β positions of the inner thiophene rings. The heterocyclic sulfur atoms participate very slightly in spin delocalization. In other words, a spin density is preferentially distributed along the carbon backbone as it takes place in the cation-radicals of the smaller oligomers and thiophene itself (Alberti et al. 2003, references therein). However, the anion-radical from this sexithiophene is characterized with significant participation of the heterocyclic sulfur atom in spin delocalization. Such a difference might be decisive for the ratio of cis and trans isomers of cation and anion-radicals from thiophene and its oligomers.

As established, 4,5,9,10-tetrahydropyrene yields the cation and anion-radicals in the form of an equilibrium mixture of conformers (Iwaizumi and Isobe 1975; Scheme 6.25).

The activation energy of the mutual interconversion depends on the nature of the charge of the ion-radical. For the cation-radical, it is half of that for the anion-radical. The authors emphasize that the reaction proceeds through an intermediary planar structure in which the methylene groups of the saturated ring are hyperconjugated with the neighboring aromatic rings. The methylene groups stabilize cations to a greater extent than anions. Therefore, the hyperconjugation lowers the system energy in cations far more than in anions. This is the reason why the temperature dependence of the ESR spectra points to a greater facility of conversion of one isomer into the other for the cation-radical when compared to that of the anion-radical.

A similar reaction was observed in the series of 1,2,3,6,7,8-hexahydropyrene cation and anion-radicals (Pijpers et al. 1971). For example, at very low temperatures, ENDOR spectra revealed the formation of two cation-radical isomers and only one anion-radical isomer (Maekelae and Vuolle 1985).

A complete silicon analog of cyclohexane, cyclohexapermethyl silane, exists in a mobile chair conformation (Bock et al. 1979). In the cation-radical, the inversion rate is much more lower than

in the anion-radical. The reason for such a behavior seemingly lies in the electron properties of the ion-radicals. The one-electron oxidation touches the HOMO of the neutral molecule and evidently enhances the initial overlapping of silicon orbitals. In one-electron reduction, the incoming electron populates the lowest orbital probably composed of earlier unoccupied *d* atomic orbitals of silicon. This leads to ring conjugation of the *d*, π type, and the system tends to flatten. The flattened conformation is similar to the one shown in Scheme 6.1 between the invertomers.

One-electron removal from thianthrene also enforces conjugation within the internal electronic system and leads to the flattening of the molecular carcass. If the neutral parent molecule is bent, the cation-radical becomes considerably flattened (Bock et al. 1994).

It is also worthwhile to compare the ferrocenyl ethylene (vinylferrocene) anion-and cation-radicals. For the cyano vinylferrocene anion-radical, the strong delocalization of an unpaired electron was observed (see Section 1.2.2). This is accompanied with effective cis→trans conversion (the barrier of rotation around the –C=C– bond is lowered). As for the cation-radicals of the vinylferrocene series, a single electron remains in the highest MO formerly occupied by two electrons. According to photoelectron spectroscopy and quantum mechanical calculations, the HOMO is mostly or even exclusively the orbital of iron (Todres et al. 1992). This orbital is formed *without* the participation of the ethylenic fragment. The situation is quite different from arylethylene radical cations in which all π orbitals overlap. After one-electron oxidation of ferrocenyl ethylene, an unpaired electron and a positive charge are centered on iron. The –C=C– bond does not share the π-electron cloud with the $Fe^{+\bullet}$ center. As a result, no cis→trans conversion occurs (Todres 2001).

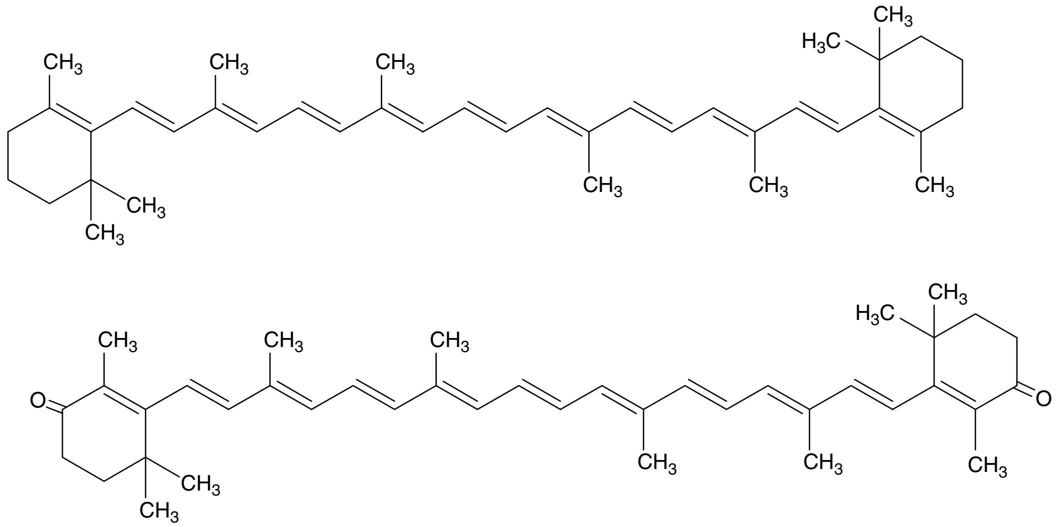
Unexpectedly, the analysis of the MOs of the cation-radical from β-cyano vinylferrocene reveals the possibility for cis→trans conversion if more than one-electron oxidation takes place. Namely, the cation-radical has an MO, which is four levels higher in energy than the one occupied by the single electron, that is centered on the cyanoethylene fragment (Todres et al. 1992).

In a similar manner, introduction of the ferrocenyl group drastically changes the reactivity of the mesityl enol ester cation-radicals. These cation-radicals undergo a bond scission in solution according to the following equation (Mes = mesityl):

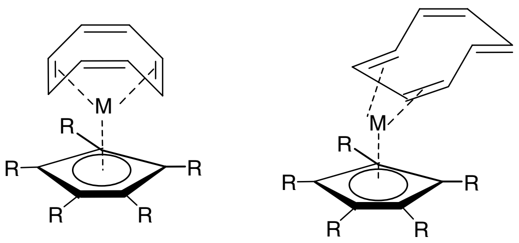
$$[Mes_2C{=}C(R^1)O\text{-}C(O)R^2]^{+\bullet} \rightarrow Mes_2C{=}C(R^1)O^+ + {}^{\bullet}C(O)R_2$$

The reaction takes place if R^1 is *t*-Bu and R^2 is $-C_6H_4N(CH_3)_2$-*p*. If R^1 is still *t*-Bu, but R^2 is Fc (ferrocenyl), no cleavage occurs (Schmittel et al. 2001). The ferrocenyl-containing cation-radical is apparently a persistent ferrocenium type of species. Intramolecular activation of the scission with ferrocene as a redox unit is not operative.

While considering the rotation around double bonds in ion-radicals, some data on isomerization in a confined environment should be supplemented. This is important for the understanding of catalytic actions of zeolites and molecular sieves. Gao et al. (2004) reported results of their ESR, UV, and high-performance liquid chromatography (HPLC) studies on isomerization of carotenoids on the action of Fe-MSM-41 molecular sieves. The average pore size of these sieves is 0.38 nm. The carotenoids investigated (all-trans β-carotene and all-trans canthaxanthin) have the chain length of approximately 0.25 nm and they can readily diffuse into such large pores. The structures of these carotenoids are depicted in Scheme 6.26. On contact with Fe-MSM-41, both carotenoids are oxidized by ferric ion of the sieves and transform into corresponding cation-radicals. The cation-radicals undergo trans→cis isomerization. However, selectivity of this process differs. The β-carotene- and the canthaxanthin cation-radical undergo preferential rotation around C_{13}–C_{14} and C_9–C_{10} double bonds, respectively. Under the conditions of electrolysis (with no participation of sieves), rotation around C_9–C_{10} double bond is typical for both the cation-radicals. Gao et al. (2004) ascribe this difference to the variation in location of these cation-radicals with respect to the MSM pore. The β-carotene cation-radical finds its way into the MSM pore and adjoins to the inner surface of the sieve pore. The most compact location of the cation-radical is provided when only cis-C_{13}–C_{14} double bond acquires the trans configuration. As to the canthaxanthin cation-radical, it keeps its



SCHEME 6.26



SCHEME 6.27

usual C_9–C_{10} trans configuration because it cannot penetrate into the pore. This cation-radical bears the carbonyl groups that form hydrogen bonds with the silanol groups of the sieve on the external surface or at the pore entrance. The canthaxanthin cation-radical is fixed on the surface or stopped at the entrance of the pore. Because the canthaxanthin chain is distal from the inner surface of the pore, it can rotate freely. Therefore, the relative amounts of the trans isomer are similar to those observed after one-electron oxidation in the absence of sieves.

Scheme 6.27 considers other, formally confined, conformers of cycloocta-1,3,5,7-tetraene (COT) in complexes with metals. In the following text, M(1,5-COT) and M(1,3-COT) stand for the tube and chair structures, respectively. M(1,5-COT) is favored in neutral (18-electron) complexes with nickel, palladium, cobalt, or rhodium. One-electron reduction transforms these complexes into 19-electron forms, which we can identify as anion-radicals of metallocomplexes. Notably, the anion-radicals of the nickel and palladium complexes retain their M(1,5-COT) geometry in both the 18- and 19-electron forms. When the metal is cobalt or rhodium, transition in the 19-electron form causes quick conversion of M(1,5-COT) into M(1,3-COT) form (Shaw et al. 2004, reference therein). This difference should be connected with the manner of spin–charge distribution. The nickel and palladium complexes are essentially metal-based anion-radicals. In contrast, the SOMO is highly delocalized in the anion-radicals of cobalt and rhodium complexes, with at least half of the orbital residing in the COT ring. For this reason, cyclooctateraene flattens for a while and then acquires the conformation that is more favorable for the spatial structure of the whole complex, namely, M(1,3-COT) (see Schemes 6.1 and 6.27).

Naturally, when a molecule loses or acquires one electron, the inner reorganization energy also changes. This can provide a driving force for the conformational transition. Thus, the one-electron oxidation of 9,10-bis(*N*,*N*-dimethylamino)anthracene evokes so significant an increase in the inner reorganization energy that it occurs to be sufficient for the distortion of the molecular framework. Namely, the neutral species possesses an undistorted ring system. The dimethylamino groups are pyramidal in nitrogen and turned out of the anthracene plane. The one-electron oxidation generates two conformers. One of them contains the dimethylamino groups partially turned out into the plane of the anthracene system, and this system is somewhat distorted. The second conformer is distinguished by the bending of the central ring of anthracene to form a boat with the two planar dimethylamino groups on the same side of the molecular carcass (Gruhn et al. 2006b).

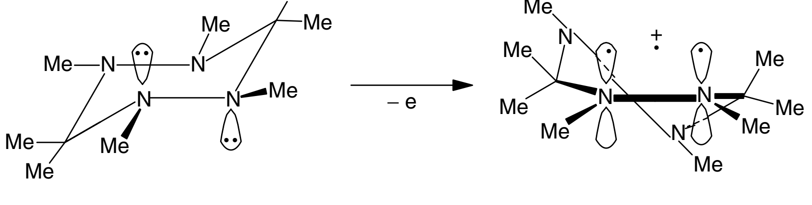
One-electron oxidation of 1,1′-biphenyl-4,4′-(*N*,*N*′-tetra-aryl)diamines, a classic polyarylamine-based hole transport materials, was studied theoretically (Malagoli and Bredas 2000) and experimentally (Low et al. 2004). As it turned out, these cation-radicals keep the biphenyl group planar, with rotation of the peripheral aryl groups about the N–C_{aryl} bonds to positions approximately orthogonal to the biphenyl plane. It is the reorganization energy that is responsible for the structural changes associated with the transition of the initial uncharged molecules into their cation-radicals.

Formation of odd-electron even-center bonds may also serve as a driving force in conformational transitions of organic ion-radicals. The nature of such bond has been considered in Section 3.2.3 and several specific stereochemical examples were analyzed.

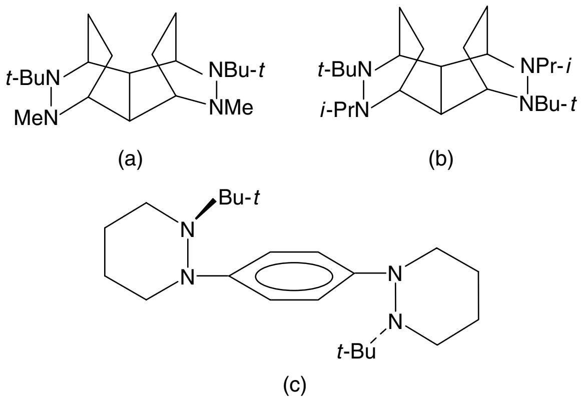
In the case of two pairs of nitrogen atoms within a six-membered saturated ring, a cation-radical is formed whose ESR spectrum contains signals of only two (not four) nitrogen atoms (Nelsen et al. 1975). In other words, the unpaired electron is localized in one hydrazine unit of tetramethyl- or tetraethyl-*sym*-hexahydrotetrazine. Intramolecular electron exchange between the two hydrazine halves of the cation-radical cyclic molecule either does not take place at all or goes out of the ESR timescale. Hence, one-electron oxidation of the tetrazines gives rise to the cation-radicals of a specific conformation. In this conformation, only two neighboring nitrogen atoms are capable of delocalizing the unpaired electron. Scheme 6.28 explains this inference; the important feature is the suspension of three electrons in the field of two nitrogen atoms.

Removal of an electron from a hydrazine unit changes the lone-pair orbital occupancy from four to three, which has a large effect on the preferred geometry with respect to the nitrogen atoms. The formation of a three-electron bond has also been demonstrated in the cation-radical of octamethyl-1,2,4,5-tetra-aza-3,6-disilacyclohexane. In this cation-radical, the spin density is distributed only between two of the four nitrogen atoms. There is a pronounced interaction between the unpaired electron and protons of the methyl groups joined to these two nitrogen atoms. These conformational changes, which take place during the transformation of neutral hydrazines or bicyclic azo compounds into cation-radicals, have also been observed in a wide range of derivatives. These changes seemingly have a general character (Williams et al. 1988, Nelsen et al. 1988a).

The conformational changes also explain the slow electron transfer between two hydrazine moieties separated by a bridge (Gleiter et al. 1996, Nelsen et al. 1975, 1976, 1997b). In all the cases, the inner reorganization energy is high when electron transfer occurs. Particularly, when the unpaired electron is transferred from the planar hydrazine cation-radical unit to the tetrahedral



SCHEME 6.28



SCHEME 6.29

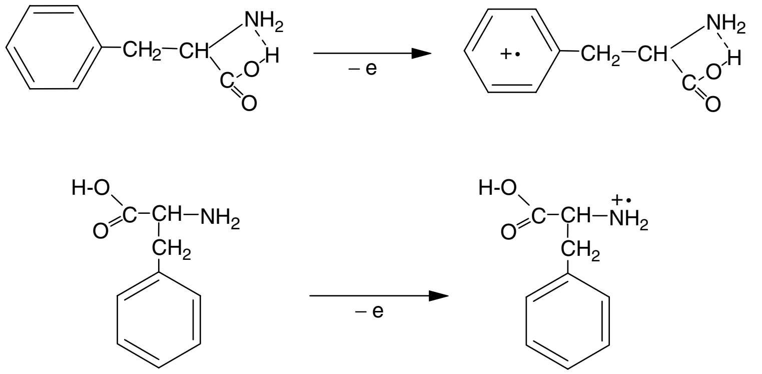
neutral hydrazine unit, large conformational changes take place. It is noteworthy to mention that although the electron-transfer barrier is sensitive to the inner reorganization energy on electron removal, it is especially sensitive to the effect of substituents attached to nitrogen. Solvation of the bridge between two hydrazine units is also too large to be ignored (Nelsen et al. 2001). Slight structural modifications result in changes of intramolecular electron-transfer constants, and these changes are large enough to be measured by dynamic ESR. The three structures in Scheme 6.29 illustrate this statement.

The change from *N*-methyl- (structure a of Scheme 6.29) to *N*-isopropyl substitution (structure b) lowers the electron-transfer barrier (Nelsen 1997, p. 171). The *p*,*p*′-phenylene-linked system (structure c) features fast electron transfer under comparable conditions. The cation-radical from the last bis-hydrazine is instantaneously localized in contrast to the cation-radical from tetramethyl-*p*-phenylenediamine, which is delocalized (Nelsen et al. 1996, 1997a, 1998b; Valverde-Aguilar et al. 2006).

The fast electron transfer mentioned for the *p*-phenylene-linked system results in the transfer of the three-electron two-nitrogen unit from one-hydrazine ring to the other. Such *superexchange* transfer is a specific phenomenon. As found by Nelsen and Ismagilov (1999), this bis(hydrazine) cation-radical is significantly ion paired with PF_6^- counterion in the methylene chloride solution. The counterion *touches* both hydrazine fragments, but the distance between the N∴N linkage and PF_6^- is permanently shorter than that between N—N and PF_6^-.

Conformational transition of amino acids is especially important in biomedical aspects. Thus, transformation of methionine into cation-radical initiates a sequence of biochemical reactions leading to the development of diseases such as glaucoma (Kantorow et al. 2004) and Alzheimer disease (Hou and Zagorski 2006). The methionine cation-radical (the cation-radical of 2-amino-4-(methylthio)butanoic acid) exists in several forms: open-chain protonated, open-chain deprotonated, and cyclic with the three-electron two-center bond between sulfur and nitrogen. All the forms are in equilibrium and the participation of the cyclic form is predominant. At a high pH of the medium, all the cation-radicals exist in the cyclic form. Evaluation of the polarization pattern yields the following spin-density distribution (ρ_i) in the cyclic cation-radical: $\rho_N = 0.36$, and $\rho_S = 0.64$ (Goez and Rozwadowski 2000). A similar situation is achieved in the cysteine cation-radical (the cation-radical of 2-amino-3-mercaptopropanoic acid). The sulfur and nitrogen atoms form the three-electron two-center bond, closing the cycle; in the cycle, $\rho_N = 0.40$ and $\rho_S = 0.60$ (Sutherland et al. 2007).

The formation of intramolecular hydrogen bonds can also anchor specific conformations of the amino acid cation-radicals. Using a combination of resonant two-photon laser ionization and



SCHEME 6.30

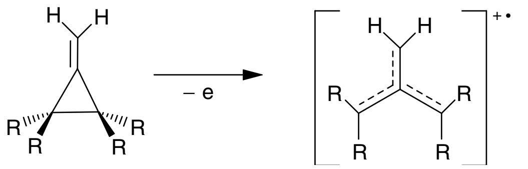
time-of-flight mass spectrometry, Lee et al. (2007) selectively ionized conformers of phenylalanine and studied the fate of the cation-radicals formed. The conformers were distinguished by mutual orientation of the amino and carboxylic groups that led to the formation of two kinds of cation-radicals. When the COOH and NH_2 groups were brought closer together, the COOH → NH_2 hydrogen bond was formed. As a result, the carbonyl hydrogen holds the lone electron pair of the amine nitrogen tightly in the hydrogen bond. On oxidation, the electron is removed solely from the phenyl ring, leaving behind a nearly whole cationic charge. The cation-radical bearing $(Ph)^{+\bullet}$ moiety is formed. When the COOH and NH_2 groups were spaced apart, the amine lone electron pair remained free and one-electron oxidation proceeded in the conventional way, presumably at the expense of the amino group. The cation-radical bearing $(NH_2)^{+\bullet}$ moiety is formed. Scheme 6.30 illustrates this difference between the cation-radical conformers. It is worth mentioning that only $(Ph)^{+\bullet}$ conformer forms photoinduced fragment peaks. The *normal* $(NH_2)^{+\bullet}$ conformer maintains some extent of stability.

6.5 SPACE STRUCTURE AND SKELETAL ISOMERIZATION OF ION-RADICALS

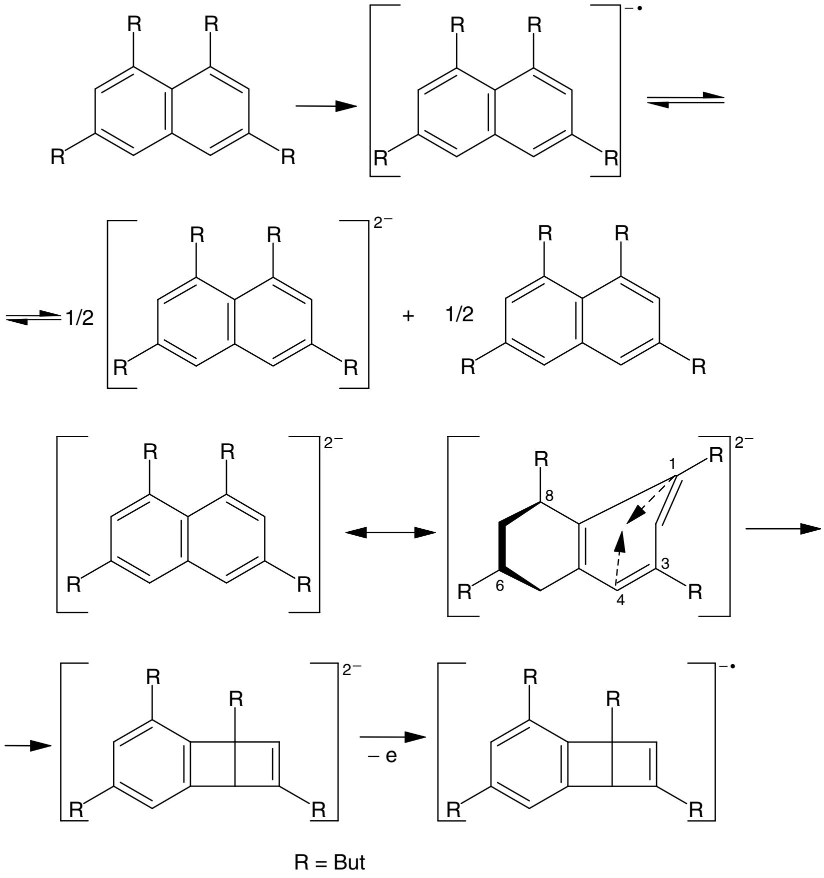
Steric factors are often responsible for skeletal isomerization in ion-radical states. The simple example in Scheme 6.31 illustrates the effect of steric congestion on activation energy of this kind of isomerization and depicts the transition of 2,2,3,3-tetramethylmethylenecyclopropane into 1,1,2,2-tetramethyltrimethylenemethane cation-radical. The rearrangement is brought about by one-electron oxidation of the substrate and represents an entirely barrierless process. Interestingly, methylenecyclopropane (bearing no methyl groups) is protected from such a spontaneous collapse by a barrier of 7.4 k · J mol^{-1} (Bally et al. 2005).

Reduction of poly(butyl)naphthalenes with sodium–potassium alloy in ether causes their isomerization (Goldberg et al. 1976). The reduction of 1,3,6,8-tetra(*tert*-butyl)naphthalene produces an anion-radical, which disproportionates yielding the initial tetrabutylnaphthalene and corresponding dianion (Scheme 6.32).

The isomerization shown in Scheme 6.32 involves two intermediary dianions and not the direct conversion of the initial anion-radical into the final one. However, what is the driving force for this isomerization? The molecule of 1,3,6,8-tetra(*tert*-butyl)naphthalene is nonplanar: the *tert*-butyl group and carbon atom at position 1 of the naphthalene skeleton lie off the plane of the molecule. The corresponding anion-radical has the same stereochemical peculiarity (Goldberg 1973). Such bending removes the steric strain but, naturally, decreases the degree of the π-electron delocalization over the neutral molecule. As for the anion-radical, its unpaired electron delocalizes less effectively than the anion-radical of the unsubstituted naphthalene. Bending of the naphthalene skeleton



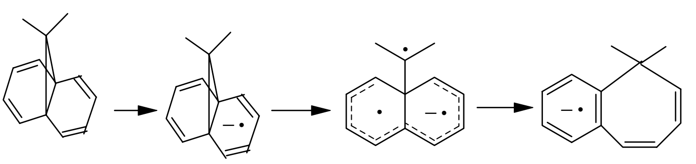
SCHEME 6.31



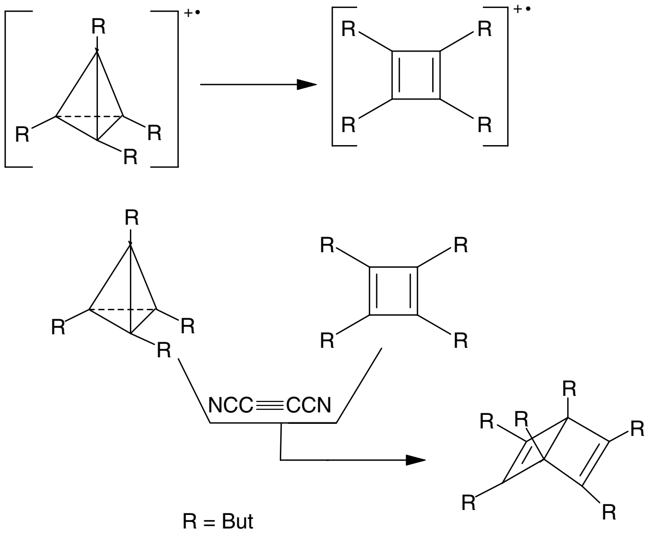
SCHEME 6.32

increases the overlapping of orbitals of atoms 1 and 4. The addition of two extra electrons increases the order of the ordinary bonds. Atoms 1 and 4 come closer to each other. Their bonding becomes possible. This facilitates the formation of the dianion and then the anion-radical in the form of the skeletal isomer.

One-electron reduction of a norcaradiene derivative produces the corresponding anion-radical. The conditions of the odd-electron delocalization in this anion-radical are less favorable than in its skeletal isomer. According to calculations, the incorporation of the unpaired electron in the nonatetraenyl π system lowers the energy content by 0.62β. However, the anion-radical initially formed is less stable than the benzotropylidene anion-radical. The latter is the end product of the isomerization (Gerson et al. 1978; Scheme 6.33).



SCHEME 6.33

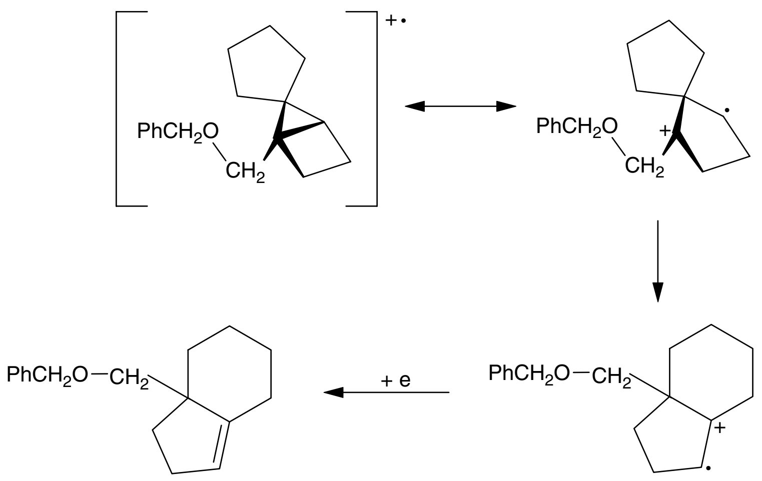


SCHEME 6.34

This conversion is directed so as to create the most favorable conditions for the delocalization of the unpaired electron within the aromatic nucleus. It is worth noting here that thermal treatment (150–190°C) also initiates isomerization of the initial neutral molecule of norcaradiene into the benzotropylidene system. At the same time, the reductive transformation of Scheme 6.33 proceeds smoothly even at negative temperatures. Under comparable reaction conditions (25°C), the rate of conversion of the neutral molecule is 15 orders lower than that of the anion-radical.

As to the cation-radical version of this isomerization, there are testimonies on the transition of the norcaradiene carcass into the cycloheptatriene skeleton. Calculations at the B3LYP level shows that cycloheptatriene cation-radical is more stable than norcaradiene cation-radical by ca. 29 kJ · mol^{-1} (Norberg et al. 2006). Hydrocarbon ion-radicals with strained ring structures have a tendency to undergo facile rearrangement to enforce the unpaired electron delocalization and release their strain energy.

Tetra(*tert*-butyl)tetrahedrane converts into tetra(*tert*-butyl)cyclobutadiene only when heated up to 140°C in vacuum. A barrier of 170 kJ · mol^{-1} separates these two isomers (Heilbronner et al. 1980). In the cation-radical state, the tetrahedrane structure converts into the cyclobutadiene structure without heating (Bock et al. 1980, Fox et al. 1982). From Scheme 6.34 it can be seen that by the action of aluminum chloride on methylene chloride, tetrahedrane forms the cation-radical of its isomer—the cyclobutadiene cation-radical and not the cation-radical of the same skeleton. The latter is more stable than the former because of more effective delocalization of the unpaired electron and positive



SCHEME 6.35

charge. Both tetrahedrane and cyclobutadiene give the same adduct with dicyanoethylene, which acts as an *adding oxidant* (Maier et al. 1982; Scheme 6.34).

Another example of cation-radical skeletal isomerization comes from works by Gerken et al. (2005) and Park et al. (2007). Particularly, Park et al. (2007) oxidized benzyloxymethylhousane to its cation radical by using electrochemically generated "Magic Blue" (tris(4-bromophenyl)-ammoniumyl). The oxidation was organized as a reversible process. Under these conditions, the initial product gave rise to the cation-radical that underwent isomerization and eventually transformed into benzoyloxymethyl bicyclononene. This final product was a sole one, and its isolated yield reached 70%. Possible mechanism of the transformation includes isomerization of the housane cation-radical leading to the formation of the distonic spiro-bicyclic counterpart and [1,2] carbon migration (see Scheme 6.35).

Adam et al. (2003) also explained their experimental results on the rearrangement of housanes through mechanisms that include the formation of distonic cation-radicals in the intermediary step. Their mechanisms were grounded by kinetic analysis (Trofimov 2004).

6.6 CONCLUSION

This chapter should be correlated to Chapters 1 through 3. There are many examples in which the ion-radical stage affects the stereochemical outcome of the entire reactions. The stereochemistry of intermediary ion-radicals obviously interrelates with the steric characteristics of the final products. Nevertheless, it would be incorrect to generalize such a interrelation. It is clear now that the important consequences of ion-radical formation are the *Z*/*E* isomerization of olefines, stereochemical changes accompanying the formation of the three-electron bonds, and skeletal isomerization in ion-radicals. The change in the steric structure governed by the conversion into the ion-radical state sometimes makes a decisive contribution to the reaction kinetics. Certain reactions involving the ion-radical stage become less sensitive to steric factors, and this may lead to highly branched compounds. The direction of a reaction along the ion-radical course may also be used to provoke conversions between stereoisomers under mild conditions.

The stereochemical opportunities of the ion-radical reactions deserve further study because of their importance in science and commercial applications. Although this branch of ion-radical organic chemistry is at present insufficiently developed, further development seems to be inevitable.

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7 Synthetic Opportunities of Ion-Radical Organic Chemistry

7.1 INTRODUCTION

The chapter aims to illustrate the advantages of ion-radical organic chemistry with respect to syntheses of desirable products. It focuses on typical synthetic approaches. The examples provided follow these guidelines:

1. The procedures given must have definite (and tangible) advantages
2. Yields of the products aimed must be high enough
3. The products themselves must be of practical interest
4. The synthetic procedures included sometimes are the only ones available for a certain compound

At this point, the author would not like to dishearten the readers who are interested in the mechanistic aspect of this book. For them, such a truism can be offered—a chemist's heart is devoted to mechanisms, but public demands for the chemist originated due to the need for new substances and reactions. Necessity is the mother of inventions! Therefore, the chapter puts forth the general ideology of pursuits in the area of ion-radical organic chemistry and examines the methodologies that have evolved in the search for solutions to synthetic problems. This chapter details achievements of ion-radical organic syntheses, not only for their scientific and practical merits, but also for the aesthetic appeal of the examples chosen and the effective solutions that have emerged.

The chapter focuses more on describing the general approaches to ion-radical syntheses and synthetic methodology, than providing a detailed account of each reaction. The examples chosen is aimed at illustrating the usefulness of the ion-radical reactions by providing preparative applications (see also some preceding sources — Linker and Schmittel 1998 and Little and Moeller 2002).

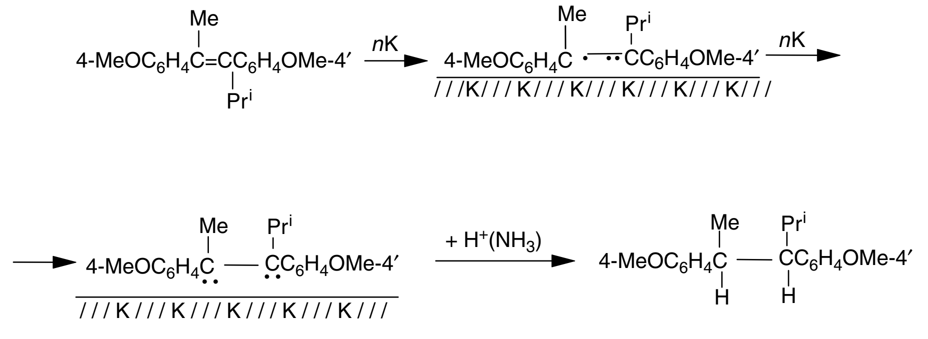
7.2 REDUCTIVE AND OXIDATIVE REACTIONS

7.2.1 Transformation of Ethylenic Ion-Radicals

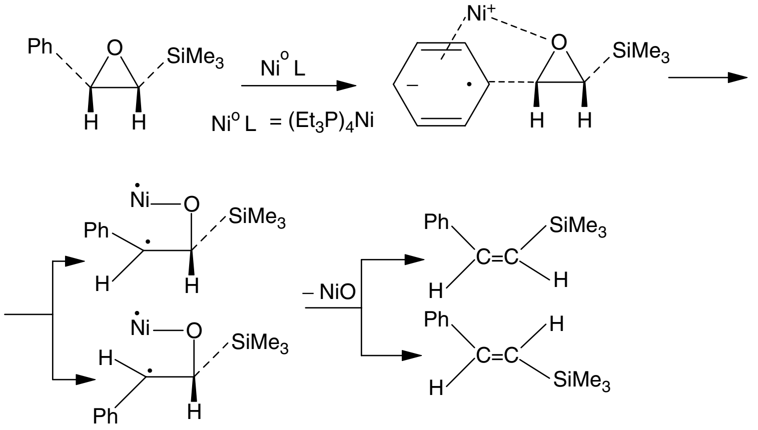
7.2.1.1 Anion-Radicals

Stilbene derivatives can be reduced with alkali metals in liquid ammonia. The reaction is usually performed in a homogeneous medium to give substituted diphenylethane compounds as a mixture of enantiomeric forms. However, there are compounds (particularly, biologically active ones) for which the stereospecificity of synthesis has decisive importance. A simple modification of the reduction method with an alkali metal in liquid ammonia was found (Collins and Hobbs 1983), which makes it possible to perform the process stereoselectively. The metal is not predissolved, as is usual, but is added in small portions without trying to make the reaction medium homogeneous. Stereoselectivity is ensured by carrying out the reduction on the surface of the metal and not in the solution bulk.

Compounds containing π systems have an affinity to the metallic surface and are arranged on the surface in a parallel manner. The ethylene bond of α-methyl-β-isopropyl stilbene is responsible for adsorption, and the substituents deviate from the metal surface. It is well known that alkali



SCHEME 7.1

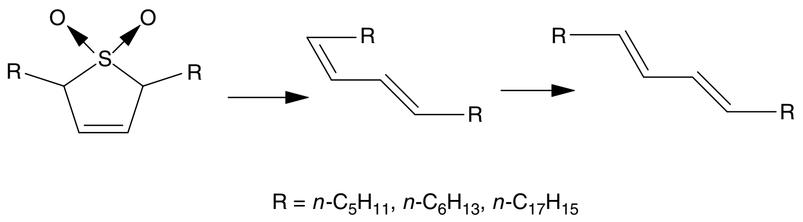


SCHEME 7.2

metals have a strong tendency to lose ions into a solvating solution. The releasing electrons jump onto the adsorbed substrate. The reaction under consideration consists of two one-electron consecutive steps resulting in the formation of a dianion. Being adsorbed, the dianion accepts two protons. Proton is a very small particle and is attracted by the dianion from the side of the negative charge localization, that is, along the metal surface. After protonation, the product obtained leaves the metallic surface. Therefore, regardless of the configuration of the initial stilbene, the reduction proceeds with a predominant formation of an erythro product (Scheme 7.1).

Eisch and Im (1977) found another simple example of a technique controlling the stereoisomeric composition of the reaction product. The technique consists of varying the time of contact between the reactants. Scheme 7.2 illustrates the transformation of β-(trimethylsilyl)styrene oxide into β-(trimethylsilyl)styrene under the action of complexes of zerovalent nickel; the reaction involves oxidation of the complex-bonded metal.

As seen from Scheme 7.2, the epoxy-ring cleavage and nickel oxidation proceed simultaneously. The nickel–oxygen bond is formed. This results in the formation of the carbon–nickel biradical in which Ph-CH• fragment can rotate freely. The cleavage of the (NiO)–C bond leads to the formation of a mixture of styrenes. At early reaction stages (30 min), *cis* and *trans* olefins are formed in 50:50 ratio. After a prolonged contact (30 h), when all possible transformations should be completed, the trans isomer becomes the main product and cis:trans ratio becomes 5:95. Such enrichment of the mixture with the trans isomer follows from the formation of the *cis*-β-(trimethylsilyl)styrene anion-radical and its isomerization. The styrene formed interacts with an excess of the nickel complex.



SCHEME 7.3

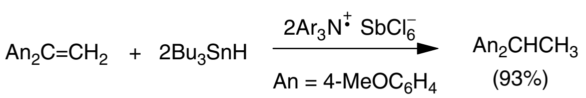
The trans isomer remains unchanged, whereas the cis isomer is converted into the trans form. The mixture thus becomes enriched with the molecules having the trans configuration. In a reference experiment, the treatment of pure *cis*-β-(trimethylsilyl)styrene with the same zerovalent nickel complex results in a 95% conversion into the trans isomer.

For isomerization, the integrity of the anion-radical must be maintained. Therefore, the isomerization degree depends on the gaseous medium of the reaction. Let us take an example. Ultrasonically dispersed potassium promotes the extrusion of SO_2 from disubstituted cyclic 3-sulfolenes to give the corresponding dienes as a mixture of *E*,*Z* and *E*,*E* forms. The *E*,*Z* and *E*,*E* isomers, respectively, are the primary and secondary products of the reaction (the *E*,*E* form is more stable thermodynamically). In dry, oxygen-free nitrogen, this ratio occurs to be 1:20. Air is chemically aggressive with respect to anion-radicals. If the reaction proceeds in air, the (*E*,*Z*):(*E*,*E*) ratio is 1:8. Consumption of the *E*,*E*-form is much greater than that of the *E*,*Z* counterpart because the *E*,*E* form was present in much more concentration. Scheme 7.3 depicts the extrusion reaction under consideration (Chou and You 1987).

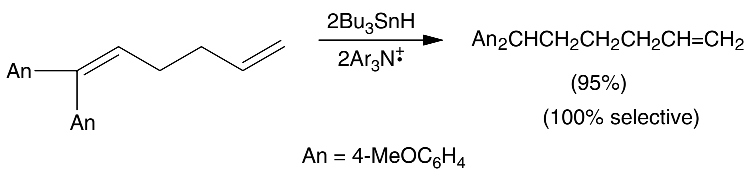
Fraser and Taube (1959), in their pioneer work, studied the interaction of Cr^{2+} or V^{2+} ions with complex salts containing a cation of methylmaleatopentamminocobalt. In acid medium ($HClO_4$ + H_2O), a redox reaction takes place. As a result of this reaction, the positive charge in the complex cation decreases by unity and the complex cation exchanges water for the methylmaleate ligand.

$$[Co(NH_3)_5(CHCOOMe)_2]^{3+} + Cr^{2+}(\text{or } V^{2+}) + H_2O \xrightarrow{HClO_4+H_2O}$$
$$[Co(NH_3)_5 \cdot H_2O]^{2+} + Cr^{3+}(\text{or } V^{3+}) + (CHCOOMe)_2$$

The liberated esterial ligand is hydrolyzed in the acid medium to give ethylene-1,2-dicarboxylic acid. However, not all the diacid formed has the cis configuration corresponding to the ligand (dimethylmaleate) in the initial complex. Along with maleic (cis) acid, fumaric (trans) acid is also formed. The higher the concentration of perchloric acid in the reaction mixture, the greater is the amount of fumaric acid. The reduction of methylfumaratopentamminocobalt ion in heavy water (D_2O), yields only fumaric acid, without an admixture of maleic acid. Interestingly, this fumaric acid does not contain C–D bonds. The electron transfer from Cr^{2+} or V^{2+} to the complex ion is accomplished by the so-called double-exchange mechanism. The reductant [Cr^{2+} or V^{2+}] transfers an electron to the bridge group (maleate) and the bridge group transfers it to the oxidant [Co^{3+}]. In this way, the bridge MeOCOCH=CHCOOMe is reduced and oxidized alternately. This is accompanied with the isomerization of *cis*-ethylenedicarboxylic ester into its trans form. When an electron is localized at the ethylenic bond, the addition of a deuteron takes place from the medium. After removal of the electron from the ethylenic bond, a D^+ ion is also detached. Redox changing of the bridge proceeds faster than H/D isotope exchange can take place. The conversion of Co^{3+} into Co^{2+} proceeds simultaneously with the replacement of ethylenedicarboxylic acid diester with a water-D_2 molecule in the inner sphere of the complex.



SCHEME 7.4



SCHEME 7.5

7.2.1.2 Cation-Radicals

Ethenic cation-radicals are also capable of rotating around the *double* bond. At the same time, the main specificity of ethylenic cation-radical reduction is the high selectivity of the reaction. One-electron oxidation was developed as a strategy for selective and efficient reduction of relatively ionizable functionalities including conjugated dienes, styrenes, and vinyl sulfides (Mirafzal et al. 1993). Reduction is highly sensitive to substrate ionizability and permits selective reduction of the more ionizable function in a difunctional compound.

Ionization of the substrates to cation-radicals is affected by means of tris(4-bromophenyl) ammoniumyl hexachloroantimonate (see Section 1.7.11). Subsequent reduction of the cation-radicals is accomplished by tributyltin hydride. For example, 1,1-di(anisyl)ethylene was efficiently (93%) reduced essentially at the time of mixing (less than 1 min), Scheme 7.4.

The case of anethole, An-CH=CH-CH_3, is interesting because of the relation between the cation-radical cyclodimerization and reduction processes. Although the rapid cation-radical dimerization of *trans*-anethole is strongly predominant, the cyclobutadimer formed is also ionized. Therefore, reductive cleavage of the dimer proceeds efficiently (80%).

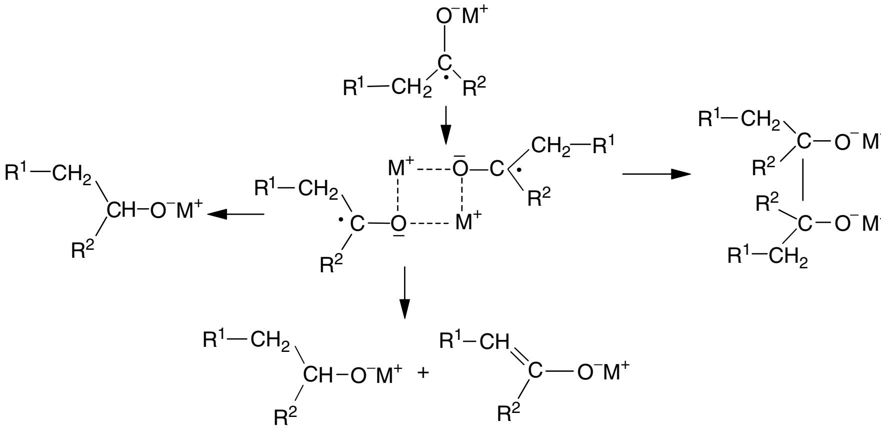
Simple alkenes such as 1-octene are completely resistant to this cation-radical hydrogenation. This makes it possible to reduce a more ionizable double bond selectively in the presence of a simple alkene moiety as illustrated for 1,1-bis(anisyl)hexa-1,5-diene in Scheme hexa-1,5,7.5 (Mirafzal et al. 1993).

Among the electron-rich alkenes, vinylsulfides are especially amenable to cation-radical reduction; an important feature is the absence of hydrogenolysis of carbon–sulfur bonds. The reduction of [(phenylthio)methylene]cyclohexane is efficient (88%), and the retention of the phenylthio group clearly contrasts with catalytic hydrogenation (Mirafzal et al. 1993). This provides versatile functionality for further synthetic operations.

The tris(4-bromophenyl)ammoniumyl hexachloroantimonate salt is not a rare reactant. It is available commercially. It can be readily prepared quantitatively from the recovered tris(4-bromophenyl)amine (Bell et al. 1969). It is also probably the most shelf stable of all the stable cation-radical salts.

7.2.2 Reduction of Ketones into Alcohols

Methods to transform ketones into alcohols are based on the use of alkali metals as electron donors. One of these methods is the Bouveault–Blanc reaction—a ketone is dissolved in alcohol and boiled with an excess of sodium. Sometimes, a ketone–alcohol mixture is rapidly added to molten sodium.



SCHEME 7.6

Sodium reacts with both ketone and alcohol. The ketone gives the desired product; the reaction with the alcohol is undesirable.

$$R^1R^2C{=}O + 2Na + R^3OH \rightarrow R^1R^2CHONa + R^3ONa$$

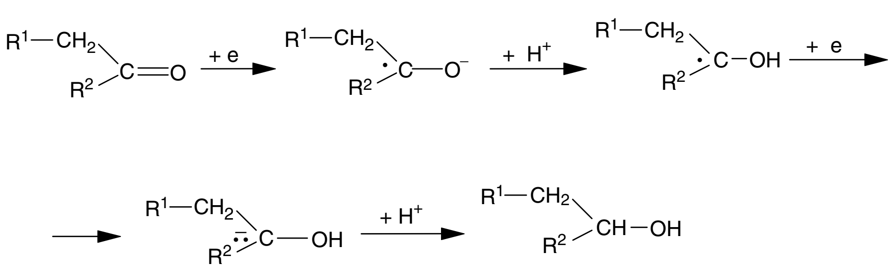
$$2R^3OH + 2Na \rightarrow 2R^3ONa + H_2$$

In a mixture of liquid ammonia with alcohol, ketoenols and pinacols are still formed along with secondary alcohols. Process selectivity was enhanced on the basis of mechanistic studies (Rautenstrauch et al. 1981). The initial stages of the reaction include the formation of ketone anion-radicals and their dimerization with a metal cation participation. This dimerization results in pinacol formation as shown in Scheme 7.6.

To prevent the dimerization and by-product formations, Rautenstrauch et al. (1981) proposed to protonate the ketone anion-radicals just at the moment of their formation. These anion-radicals contain the negatively charged oxygen atom. They protonate faster and then undergo dimerization. The resulting hydroxyl-containing carboradicals accept electrons faster and then undergo disproportionation or recombination. This leads to the suppression of ketoenol and pinacol formation.

The solvent mixture (alcohol + liquid ammonia) is not a good medium for protonation. Ammonia has a pK_a value of 34, and alcohols are characterized by pK_a values of 16–19. Hence, a proton donor should be introduced from outside. Water is not effective as a protonating agent; its pK_a value is 15.74 and close to that of alcohol. As for the ammonium cation, its pK_a value is 9.24. Therefore, ammonium chloride was proposed as a protonating additive. Besides, the addition of ammonium chloride assists buffer formation in the reaction solution. The authors used a small concentration of ammonium chloride because the metal can preferentially reduce the ketone, and not the ammonium ion ($NH_4^+ + e \rightarrow NH_3 + ½H_2$). Despite low concentrations of ammonium chloride, the protonation of the ketone anion-radical proceeds rapidly. In the presence of ammonium chloride, the reaction results are independent of the metal nature (Li, Na, K). According to the authors, in the presence of ammonium ions, the reaction proceeds as shown in Scheme 7.7.

It is important that this process results in the preferential formation of a thermodynamically stable alcohol diastereomer. The anion-radicals contain an almost undoubtedly planar $^{\bullet}C{-}O^-$ and give rise to pyramidal hydroxy carboradicals. The hydroxy carboradicals form pyramidal hydroxy carbanions, which cannot exist in the presence of ammonium cation for a long time. Therefore, the equilibrium including pyramidal inversion, probably, takes place at the step of carboradical formation, rather than carbanion formation. Transformation of a carboradical into a carbanion obviously proceeds faster than its dimerization or disproportionation. As a consequence, the reduction of an optically active ketone into an alcohol goes without racemization (Rautenstrauch et al. 1981).



SCHEME 7.7

Stereospecific ketone reduction was also observed (Giordano et al. 1985) with potassium, rubidium, and cesium (but not with sodium) in tertiary alcohols (but not in secondary or primary alcohols). The undesirable dimerization probably proceeds more readily in the case of sodium. Tertiary alcohols are simply more acidic than primary or secondary alcohols. It is reasonable to point out that the ketone-to-alcohol reduction of 3α-hydroxy-7-oxo-5β-cholic acid by alkali metals is a key step in the industrial synthesis of 3α,7β-dihydroxy-5β-cholic acid.

The dispersity or homogeneity of the reductant in a reaction system sometimes plays a decisive role. It is also important for synthetic practice. Crandall and Mualla (1986) compared reduction of 7-methylocta-5,6-diene-2-one [H_3C-$C(CH_3)$=C=CH-CH_2-CH_2-C(O)-CH_3] in THF by the action of naphthalene-sodium, on the one hand and, by sonically activated sodium on the other. In both the cases, one-electron transfer yields the anion-radical salt of the allenic ketone with sodium. However, only in the case of sonicated sodium is this salt stabilized, eventually giving H_3C-$C(CH_3)$=C=CH-CH_2-CH_2-C(OH)-CH_3 along with cyclic products (1-methyl-2-isopropylidene cyclopentanol and 1-methyl-2-isopropylcyclopent-2-enol). If naphthalene-sodium is used, only the cyclic alcohols are obtained as mentioned earlier.

7.2.3 Preparation of Dihydroaromatics

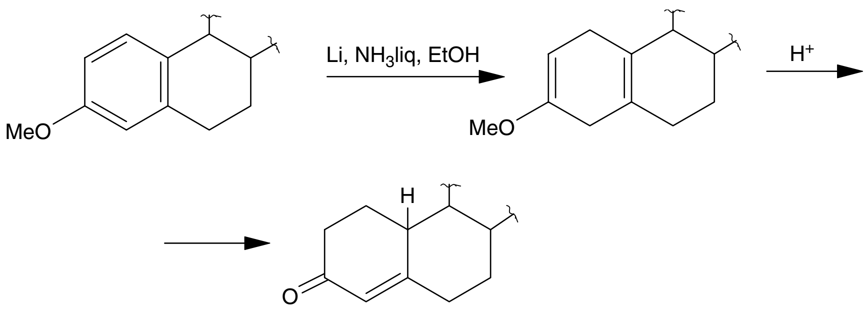
Dihydroaromatics find diverse applications. The main way to prepare them is through Birch reduction of aromatic compounds (Birch 1944, Wooster and Godfrey 1937, Hueckel and Bretschneider 1939). Aromatic compounds are hydrogenated in diethyl ether or liquid ammonia, with alkali metals as reductants and alcohols as proton sources.

An important application of Birch reaction is the synthesis of steroids containing the keto group (Scheme 7.8). The reaction, although about 70 years old, is still widely used. It has also attracted significant efforts to elucidate its mechanism and establish its regularities (see, e.g., Birch et al. 1980a, 1980b, 1981, Tomilin et al. 1980, Zimmerman and Wang 1990, 1993, Ballard et al. 2006).

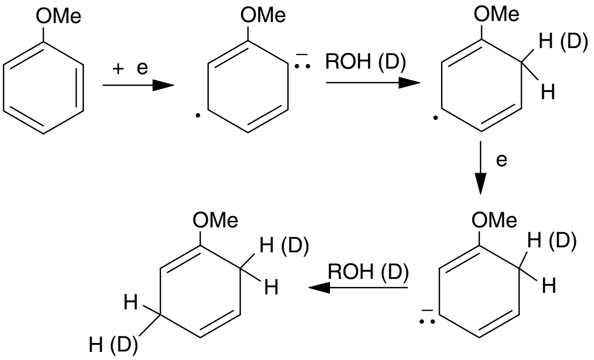
It was realized that the mechanism of Birch reduction involves protonation of the anion-radical formed by the addition of one electron to the reacting aromatic compound. This is followed by rapid addition of a second electron and protonation of the forming carbanion to yield nonconjugated alicyclic products. Protonation of the anion-radical by added alcohol is the rate-limiting stage. Recent calculations show that the ortho and meta positions in anisole are most enhanced in density by electron introduction. The para position is not appreciably affected (Zimmerman and Alabugin 2001; Scheme 7.9).

The regularities of the Birch reaction are a problem that is relevant to the aim of this chapter; bringing them together is useful to choose the right decision when planning for synthesis.

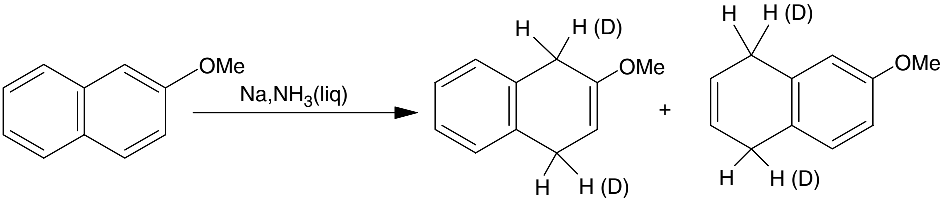
1. There is a kinetic preference in obtaining regioisomers that will contain the maximum number of alkyl or alkoxy groups on the residual double bond.
2. It is the position ortho to the maximum number of substituents that is most electron rich in an anion-radical of a starting aromatic compound. Being a less basic species, anion-radicals exhibit a more selective primary isotope effect than their more basic (and therefore



SCHEME 7.8



SCHEME 7.9



SCHEME 7.10

more reactive) carbanion counterparts. As a consequence, the deuterium enrichment in the meta position is usually higher than in the ortho position.

3. Hydrogenation of perdeuterated molecules proceeds somewhat easier than that of their protio isotopomers. Comparison of the hydrogenation heat between the anion-radicals of naphthalene and perdeuteronaphthalene demonstrated this effect. As seen in Section 2.6.2, the stability of the naphthalene anion-radical is somewhat higher than that of the perdeuterated analog. The hydrogenation of naphthalene results in some loss of aromaticity. This destabilizes the molecular system, but resistance against destabilization of naphthalene anion-radical appears to be higher than the resistance of perdeuteronaphthalene anion-radical (Ballard et al. 2006).
4. In one of the more frequently utilized Birch reactions (the reduction of alkyl/alkoxy-substituted naphthalenes), two reduction products are obtained as shown in Scheme 7.10. The acidity of the alcohol employed for protonation determines the ratio of these two products. For example, the ratio of the product hydrogenated in the substituted fused ring to the product hydrogenated in the unsubstituted fused ring was compared for methanol

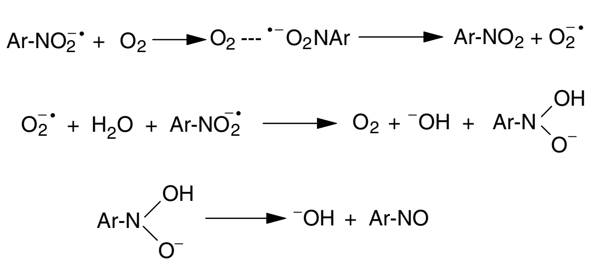
and *tert*-butanol. The ratio was found to be 2:1 in the case of methanol and 1.3:1.0 if *tert*-butanol is used (Zimmerman and Wang 1993).

5. The manner in which LUMO is distributed over the molecule to be reduced is important for the Birch reaction outcome. Aimed to prepare medications against P388 leukemia, Kim and Gevorgyan (2005) performed partial (Birch) reduction of methoxy-substituted pyrroloisoquinolines. As it turned out, C_7-methoxy derivative was selectively converted to the corresponding 5,6-dihydropyrroloisoquinoline in excellent yield. Under the same conditions, C_9-methoxy isomer reacts unselectively and for not more than 50% yield. The authors performed B3LYP calculations of both the starting molecules and revealed that the LUMO's higher density of C_7-methoxy isomer resides equally at C_5 and C_6 positions (it is C_5–C_6 bond that undergoes the selective reduction). As for C_9-methoxy isomer, the LUMO's higher density was at C_7 position only, thereby causing nonselective reduction.
6. While donor substituents assist in ortho and meta protonation, acceptor substituents direct protonation of the primary anion-radicals to the ipso and para positions. It should be emphasized that water treatment of the naphthalene anion-radical in THF leads to 1,4-dihydronaphthalene. Notably, the same treatment of this anion-radical, but σ-bound to rhodium, leads to strikingly different results. In the rhodium-naphthalene compound, an unpaired electron is localized in the naphthalene, but no protonation of the naphthalene part takes places on addition of water. Only evolution of hydrogen was observed (Frech et al. 2006). Being σ-bound to rhodium, naphthalene acts as an electron reservoir. The naphthalene anion-radical part reacts with a proton according to the electron-transfer scheme similar to the anion-radicals of aromatic nitro compounds (see Scheme 1.14).

A special case of anion-radical protonation—the protonation of the nitrobenzene anion-radical—deserves some special consideration. The main part of the electron density is concentrated within the nitro group of this anion-radical (see Section 1.2.1). It is the nitro group that the proton attacks. Such an attack helps enhance the population of the nitro group with an unpaired electron. As a result, the ring protonation becomes prohibited. The nitro group bearing an unpaired electron interacts with a proton. This should lead to reduction of $NO_2^{-\bullet}$ group, however, unexpectedly, a proton captures an electron and goes away as hydrogen. Alkali salts of the nitrobenzene anion-radical almost quantitatively recover nitrobenzene on protonation (Russell and Bemis 1967). The evolution of hydrogen under such conditions has been documented (see Section 1.3.1).

This specific direction of *protonation* might be caused due to the inclusion of a proton in the chelate between the two oxygen atoms of $NO_2^{-\bullet}$ group. The negative charge of $NO_2^{-\bullet}$ group attracts a proton. Being included in the unpaired electron delocalization within the chelate, a proton seizes an electron and departs as a small radical particle •H.

In *o*-nitrophenol, one of these chelating oxygen atoms is immobilized at the expense of the intramolecular hydrogen bond between the neighboring nitro and hydroxy groups. Protonation of the *o*-nitrophenol anion-radicals does result in the nitro group reduction. The presence of oxygen significantly aids this reduction (Bil'kis and Shteingarts 1982; Scheme 7.11).

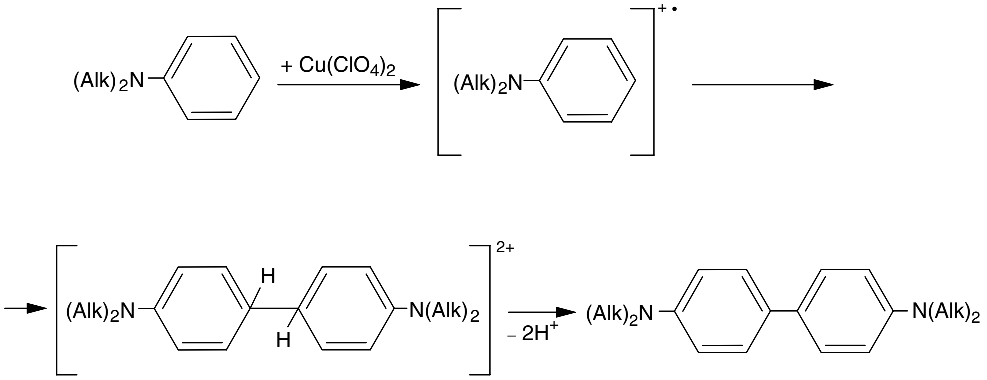


SCHEME 7.11

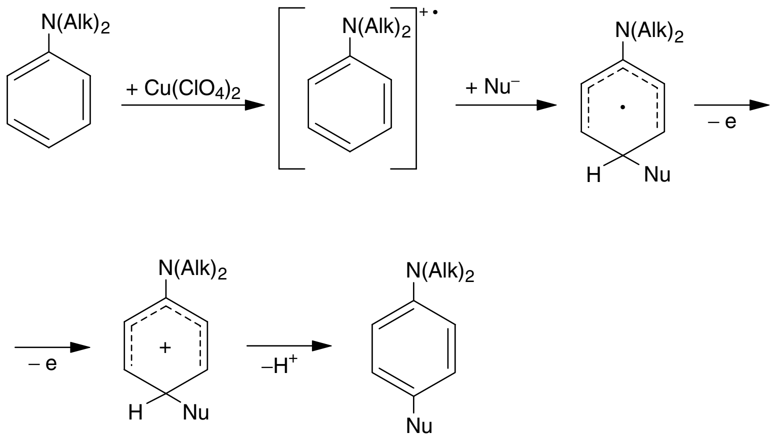
7.2.4 Synthetic Suitability of (Dialkylamino)benzene Cation-Radicals

Benzenes having *N*,*N*-dialkyl groups (*N*,*N*-dialkylanilines) readily form the corresponding cation-radicals on oxidation with cupric perchlorate. The reactions proceed at room temperature in air. AN (a solvent) was used without preliminary drying. The final products were *N*,*N*,*N'N'*-tetralkylbenzidines, which were formed in 85–90% yields (Kirchgessner et al. 2006). On monitoring the reaction by UV spectroscopy, the authors established formations of dialkylaniline cation-radicals and then dihydrodimers. The latter lost protons giving rise to final benzidines. Scheme 7.12 illustrates the sequence of the transformations observed. The reactions allow preparing benzidines in one stage and are effective in terms of yields and availability of starting materials. Practice strongly needs in benzidine derivatives because of their applications to light-emitting diodes, field-effect transistors, organic solar cells, and photoconductors.

Nucleophiles, when they are used in the presence of cupric perchlorate, capture the cation-radicals initially formed. Instead of benzidines, the para-substituted dialkylanilines were obtained. In this a manner, *N*,*N*-dialkylanilines with halo or thiocyanato moieties in para positions were prepared in good yields under the same (simple) conditions. Scheme 7.13 illustrates the sequence of the transformations observed. The products are useful intermediates in the synthesis of dyes, drugs, and color cinema formulations.



SCHEME 7.12



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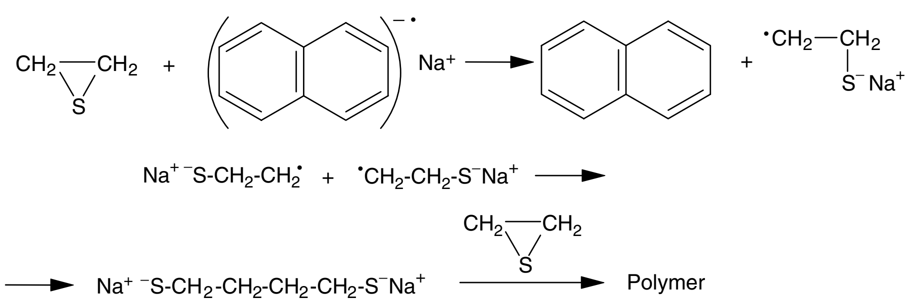


SCHEME 7.14

7.3 ION-RADICAL POLYMERIZATION

7.3.1 Anion-Radical Polymerization

Ethylene and propylene episulfides polymerize in THF at 0–70°C in the presence of sodium naphthalene, and (importantly) the polymer contains no naphthalene residues. The reaction involves one-electron transfer followed by dimerization of the resulting radical to give a dithiolate ion. This ion then polymerizes an episulfide by anionic mechanism (Boileau et al. 1967; Scheme 7.14).

When an anion-radical initiator bears chemically active groups, it is incorporated into the polymer chain. For instance, the polymer obtained from styrene under initiation by 9,10-anthraquinone anion-radical, that is, anthrasemiquinone, contains oxyanthracenyl (ethereal) fragments (Karpinets 2004). It is seemingly suitable to introduce functional groups into macromolecules through this way.

Another mode to initiate polymerization consists of reactions between anion-radicals and amines as proton donors. Thus, polymerization was provoked by photoirradiation of AN solution, containing methyl methacrylate, triethylamine, and 4-nitroanisole. If 4-nitrobenzonitrile was used instead of 4-nitroanisole, the monomer polymerization did not set in (Norambuena et al. 2004). Triethylamine reacts with both nitro compounds. As proven, this results in the formation of triethylamine cation-radical and anion-radical of 4-nitroanisole or 4-nitrobenzonitrile, within the geminate ion-radical pair. The following reaction consists of proton transfer from the cation-radical to the anion-radical. Being an electron-withdrawing substituent, the C≡N group decreases the electron density at $NO_2^{-\bullet}$ group and proton transfer becomes difficult. On the contrary, CH_3O group increases the electron density at $NO_2^{-\bullet}$ group and proton transfer is promoted. By eliminating a proton, $(CH_3)_2N^{(+\bullet)}–CH_3$ transforms into $(CH_3)_2N^{(+\bullet)}–CH_2^{(-)}$. The latter attacks methyl methacrylate and thus initiates polymerization.

In many cases, homopolymerization can be initiated by the anion-radicals of the monomers themselves. Of course, such monomers must have pronounced electron affinity (EA) and be stabilized by delocalization of an unpaired electron. Typical examples are represented by the anion-radicals of 1,1-dicyanoethylene (EA = 1.36 eV) and methyl or ethyl 2-cyanoacrylates (EA = 1.08 eV). In all of these anion-radicals, an unpaired electron is primarily localized on C atom of the CH_2 segment and characterized by appreciable resonance stabilization (Brinkmann et al. 2002). These anion-radicals are nucleophilic and attack the neutral monomers to initiate polymerization.

These examples demonstrate the well-known process of polymerization initiated by anion-radicals. Our next consideration is devoted to an unusual case of initiation. Intercalation of fullerenes by metals results in the formation of fullerene-metal derivatives. Paramagnetic metallofullerenes (anion-radicals) are the fullerenes doped with endohedral metal. According to calculations and structural studies, LaC_{82}, for example, contains La in the center of one hexagonal ring of the fullerene cage (Akasaka et al. 2000, Nishibori et al. 2000, Nomura et al. 1995). Intrafullerene electron transfer in metallofullerenes is possible (Okazaki et al. 2001).

It was found that the intercalation of C_{60} fullerene by an alkali metal in stoichiometric ratio (1:1) gives rise to the formation of anion-radical salts, namely, KC_{60}, RbC_{60}, and CsC_{60} (Bommeli et al. 1995, Btouet et al. 1996). On slow cooling of the intercalation products, [2 + 2] cycloaddition of the fullerene species that is neighboring a crystal lattice occurs. Linear chain fullerenic polymers are formed. These polymers are stable in air, insoluble in THF, and possess metallic conductivity. They depolymerize only on heating above 320°C.

A possible explanation of this conductivity assumes that polymerization of fullerene anion-radicals results in the formation of a long conjugated chain. This is why the conduction electrons can move along the chain.

Interestingly, if the C_{60} fullerene doped by alkali metals is rapidly cooled down to the liquid nitrogen temperature, polymerization does not occur. Only monomeric anion-radical salts are obtained. Warming up these monomers to 80–160 K results in dimerization; polymerization does not take place. The dimer $(KC_{60})_2$ is dielectric (Pekker et al. 1995). It has been shown that the tris(anion)-radical $C_{60}^{3-\bullet}$ can polymerize too. Particularly, Na_2CsC_{60} forms a polymer that maintains superconducting properties (Mizuki et al. 1994).

7.3.2 Cation-Radical Polymerization

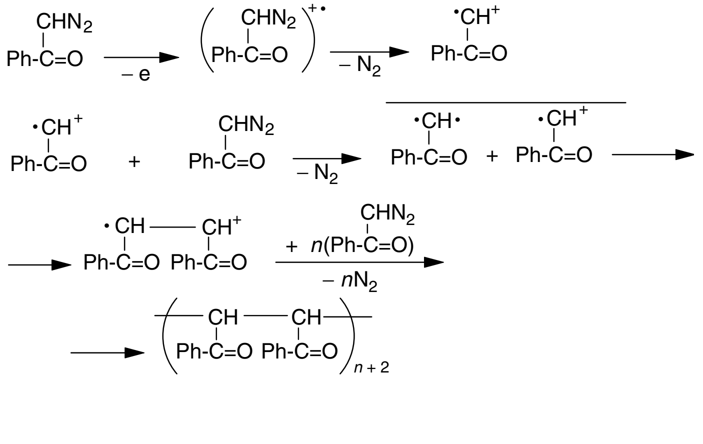
7.3.2.1 Formation of Linear Main Chains

The linear cation-radical polymerization of diazoacetophenone has been described (Jones 1981). The reaction proceeds with the evolution of nitrogen and attracts some interest as a route to porous plastic materials.

Tris(4-bromophenyl)ammoniumyl hexafluoroantimonate was used as an oxidant. Reacting with a great excess of diazoacetophenone in dichloromethane at room temperature, the ammoniumyl transforms into tris(4-bromophenyl)amine. This means that one-electron oxidation of the substrate takes place. Diazoacetophenone transforms into a cation-radical and gives a polymer containing only the phenylcarbonyl side groups (Scheme 7.15).

The linear polymerization of Scheme 7.15 represents an unusual case of diazoacetophenone oxidation. For instance, on the action of copper oxide, diazoacetophenone gives ketocarbene, which is involved in typical carbene reactions such as dimerization, addition to olefins, and insertion in the O–H bonds of alcohols. If the amine cation-radical is used as an oxidant instead of copper oxide, only the polymer is formed. The ketocarbene was not observed despite careful searches (Jones 1981).

The synthesis of polyaniline and copolymers of aniline with *o*-nitroaniline is aimed at obtaining an electroactive material. This material can be used, for example, as an electrode in conjunction with the magnesium electrode to construct chemical power sources. The polymers were prepared by oxidation of aniline or its mixture with nitroaniline; ammonium persulfate in aqueous hydrochloric



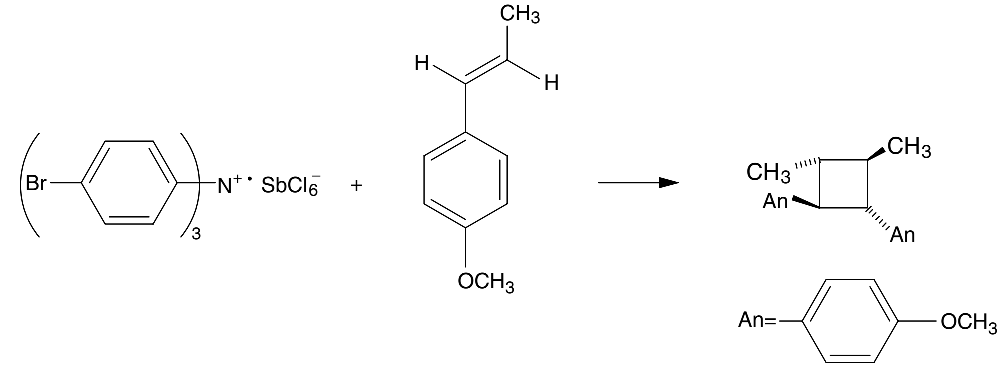
SCHEME 7.15

acid was the oxidation system. The yields of high-polymer products were in the range of 50–80%. The first stage of polyaniline synthesis was found to be the formation of $PhNH_2^{+\bullet}$ cation-radical. The mechanism of the step-by-step condensation of aniline includes quinoidization of this cation-radical and its head-to-tail coupling with the initial cation-radical. Later on, dimer deprotonation and chain lengthening take place (Koval'chuk et al. 2001).

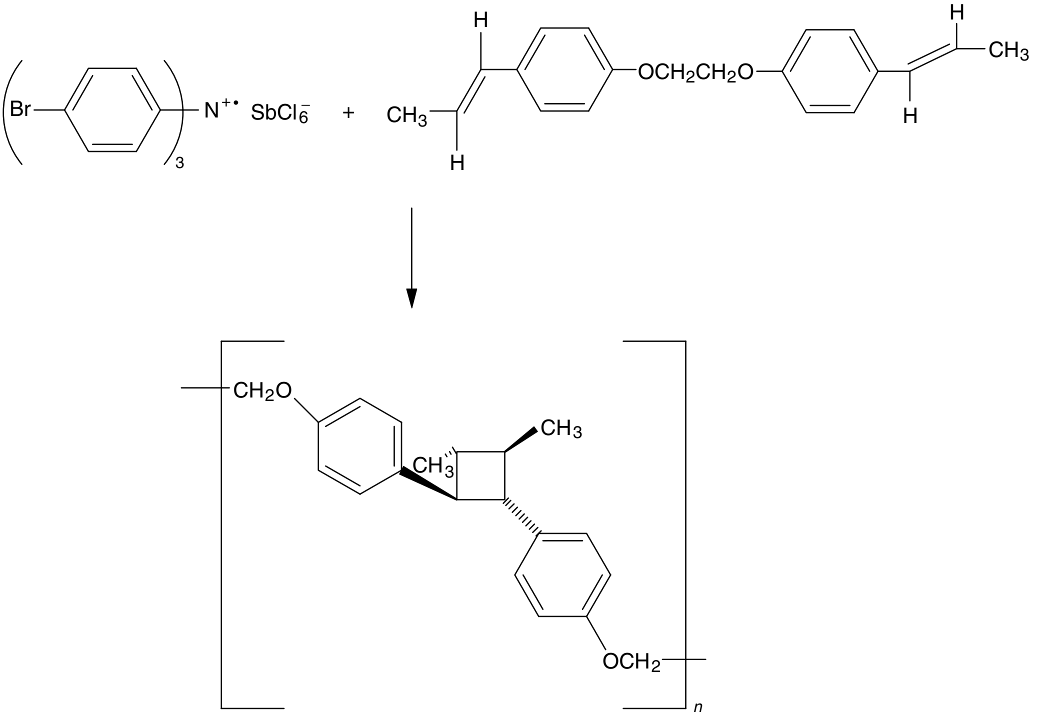
7.3.2.2 Formation of Cyclic and Branched Chains

In the presence of catalytic amounts of tris(4-bromophenyl)ammoniumyl hexachloroantimonate in methylene chloride at 0°C, *trans*-anethole is smoothly converted in less than 5 min to the cyclobutane dimer (Bauld et al. 1996; Scheme 7.16).

Under the same conditions, bis(ethylenic), a close analog of anethole gives rise to a cyclobutapolymer as shown in Scheme 7.17.



SCHEME 7.16



SCHEME 7.17

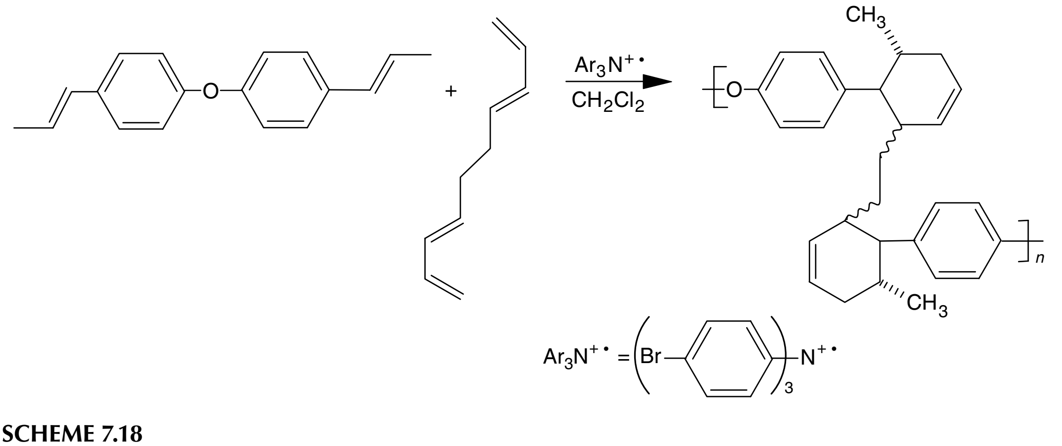
The degree of polymerization depends on the duration of the process. After 7 min, the molecular mass is equal to 9400 (the polydispersity index is 5.30). When the reaction is carried out for 15 min, the molecular mass of the polymer increases to 37,000 and the polydispersity index reaches 7.31 (Bauld et al. 1996). Depending on whether cation-radical centers arise at the expense of intramolecular electron transfer or in a stepwise intermolecular lengthening, polymerization can occur, respectively, through a chain or a step-growth process (Bauld and Roh 2002). In the reaction depicted in Scheme 7.17, both chain and step-growth propagations are involved.

Along with homopolymerization, copolymerization has also been studied within the framework of initiation by tris(4-bromophenyl)ammoniumyl hexachloroantimonate (Bauld et al. 1998a). Generally, cation-radical cycloaddition occurs more efficiently when the reactive cation-radical is the ionized dienophile (Bauld 1989, 1992). In the cited work on copolymerization, the bis(diene) was chosen to be resistant against ionization by the initiator used. As to the dienophile functionality, propenyl rather than vinyl moieties were selected because terminal methyl groups sharply enhance the ionizability of the alkene functions. The polymerization shown in Scheme 7.18 was performed in dichloromethane at 0°C.

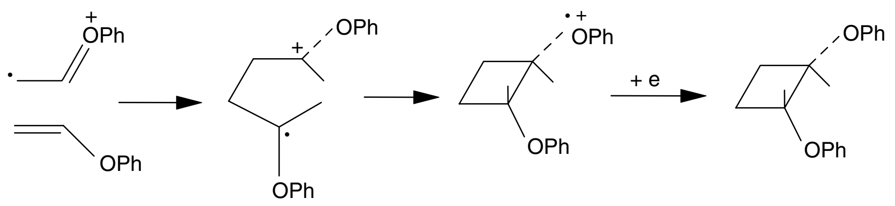
The final copolymer was obtained in 90% yield; it had a molecular weight of 10,800 and polydispersity index of 2.1. In this case, Diels–Alder copolymerization dominates over the cyclobutane homopolymerization. It means that Diels–Alder addition of the dienophile cation-radical to the diene is substantially faster than the competing addition of the dienophile cation-radical to the neutral dienophile.

Hence, cation-radical copolymerization leads to the formation of a polymer having a lower molecular weight and polydispersity index than the polymer got by cation-radical polymerization—homocyclobutanation. Nevertheless, copolymerization occurs under very mild conditions and is regio- and stereospecific (Bauld et al. 1998a). This reaction appears to occur by a step-growth mechanism, rather than the more efficient cation-radical chain mechanism proposed for poly(cyclobutanation). As the authors concluded, "the apparent suppression of the chain mechanism is viewed as an inherent problem with the copolymerization format of cation-radical Diels–Alder polymerization."

Generally, at least in theory, an important aspect of cation-radical polymerization, from a commercial viewpoint, is that either catalysts or monomer cation-radicals can be generated electrochemically. Such an approach deserves a special treatment. The scope of cation-radical polymerization appears to be very substantial. A variety of cation-radical pericyclic reaction types can potentially be applied, including cyclobutanation, Diels–Alder addition, and cyclopropanation. The monomers that are most effectively employed in the cation-radical context are diverse and distinct from those that are used in standard polymerization methods (i.e., vinyl monomers). Consequently, the obtained polymers are structurally distinct from those available by conventional methods although the molecular masses observed so far are still modest. Further development in this area would be promising.



SCHEME 7.18



SCHEME 7.19

7.4 RING CLOSURE

This section is devoted to cyclizations and cycloadditions of ion-radicals. It is common knowledge that cyclization is an intramolecular reaction in which one new bond is generated. Cycloaddition consists of the generation of two new bonds and can proceed either intra- or intermolecularly. For instance, the transformation of 1,5-hexadiene cation-radical into 1,4-cyclohexadienyl cation-radical (Guo et al. 1988) is a cyclization reaction, whereas Diels–Alder reaction is a cycloaddition reaction. In line with the consideration within this book, ring closure reactions are divided according to their cation- or anion-radical mechanisms.

Among the methods of organic synthesis, Diels–Alder reaction holds an important position. The cycloaddition of 1,3-dienes with olefins is one of the most thoroughly studied reactions in organic chemistry.

The ion-radical Diels–Alder reactions represent a new development (see, e.g., reviews by Hintz et al. 1996, Berger and Tanko 1997). These reactions initiated with ion-radicals proceed faster by several orders of rate magnitude than the corresponding conventional reactions. This section presents the most important cyclizations developed through cation- and anion-radical schemes and the scheme that includes both cation- and anion-radicals.

7.4.1 Cation-Radical Ring Closure

The cation-radicals of ethenes, which are the primary products of one-electron oxidation, differ in their reactivity from the corresponding neutral compounds. This widens the possibilities of syntheses. Primary oxidation of ethenes (photochemically, with salts of transition metals or ammoniumyl salts) makes it possible to obtain cation-radicals, which initiate reactions that are unusual for ethenes in an uncharged state. For instance, the cation-radical of phenylvinyl ether initiates head-to-head cyclodimerization as shown in Scheme 7.19 (Ledwith 1972, Farid and Shealer 1973, Kuwata et al. 1973).

The cyclodimerization depicted in Scheme 7.19 is one of the many examples concerning cation-radicals in the synthesis and reactions of cyclobutanes. An authoritative review by Bauld (2005) considers the problem in detail. Dimerization is attained through the addition of an olefin cation-radical to an olefin in its neutral form; one chain ends by a one-electron reduction of the cyclic dimer cation-radical. Unreacted phenylvinyl ether acts as a one-electron donor and the transformation continues. Up to 500 units fall per one cation-radical. The reaction has an order of 0.5 and 1.5 with respect to the initiator and monomer, respectively (Bauld et al. 1987). Such orders are usual for branched-chain reactions. In this case, cyclodimerization involves the following steps:

1. Initiation by means of one-electron oxidation of the monomer (M)

$$M + Ar_3N^{+\bullet} \rightarrow M^{+\bullet} + Ar_3N$$

2. Formation of the dimer (D) at the expense of the association between the cation-radical obtained and the initial monomer

$$M^{+\bullet} + M \rightarrow D^{+\bullet}$$

3. The chain delivery

$$D^{+\bullet} + M \rightarrow D + M^{+\bullet}\,;\, D^{+\bullet} + Ar_3N \rightarrow D + Ar_3N^{+\bullet}$$

4. The chain termination

$$2M^{+\bullet} \rightarrow (M\!-\!M)^{2+}$$

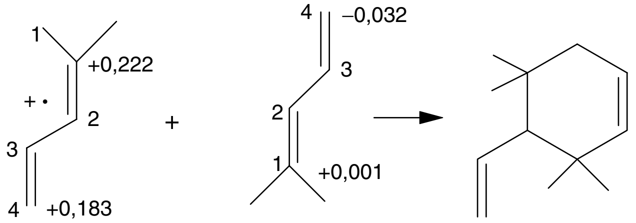
Of course, the cyclic cation-radical formed should be less stable than the alkene cation-radical (which contains a double bond that is favorable for the spin–charge scattering). However, the cation-radical product and corresponding neutral species are generated in a concerted process. The process involves simultaneous covalent bond formation and one-electron reduction of the cyclic product (Karki et al. 1997). Similar to other branched-chain processes, the cation-radical dimerization is characterized by an activation enthalpy that is not too high. These magnitudes are below 20 kJ mol^{-1} for the pair of cyclohexadiene and *trans*-anethole (p-$MeOC_6H_4CH{=}CHCHMe$, *Z*–form; Lorenz and Bauld 1987). It is clear that the cation-radical variant of cyclodimerization differs in its admirable kinetic relief. For cyclohexadiene and *trans*-anethole, catalytic factors are 10^{23} and 10^{49}, respectively (Bauld et al. 1987).

In the case of *p*-methoxystyrene (p-$MeOC_6H_4CH{=}CH_2$), the cation-radical ring closure can lead to 1,2-dianisylcyclobutane or 4-anisyl-6-methoxy-3,4-dihydronaphthalene. Thermodynamic simulations show that the former should be favored in the absence of a solvent, whereas the latter product could be stabilized by a polar solvent (O'Neil and Wiest 2006). Of course, such a solvent has to be fairly polar and not nucleophilic.

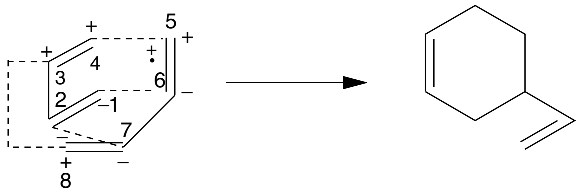
Alkylimidazolium tetrafluoroborates are, for example, ionic liquids at room-temperature that can provide an anion to stabilize an intermediate cation-radical with no possibility of nucleophilic attack on it. Ionic liquids have a huge memory effect, and their total friction is greater than that of conventional polar solvents. Thus, the total friction of 1-ethyl-3-methylimidazolium hexafluorophosphate is about 50 times greater than that of AN (Shim et al. 2007). The solvent effects of ionic liquids on ion-radical ring closures deserve a special investigation. The ring closure reactions can be, in principal, controlled by solvent effects.

Now, dienes with shielded double bonds can be involved in diene synthesis. The presence of donor groups at the double bond normally prevents its involvement in conventional Diels–Alder condensations. These reactions do take place with the cation-radicals. Cyclic adducts are formed in high yields (80–90%) and under mild conditions. Polymerization, which usually decreases the yield is inhibited completely within the framework of the cation-radical variant (Bellville et al. 1981). The stereoselectivity of the addition, which is usually typical for diene condensation, does not change in the cation-radical version and even increases. The positional selectivity also increases. The regioselectivity is enhanced, as well. Bauld et al. have discovered and explained these effects (Bellville and Bauld 1982, Bellville et al. 1981, 1983, Bauld and Pabon 1983, Pabon and Bauld 1984).

The positional selectivity is observed in those cases where a nonsymmetrically substituted diene acts as a dienophile. The more substituted double bond is involved in an ion-radical reaction, which develops according to Scheme 7.20.



SCHEME 7.20



SCHEME 7.21

Scheme 7.20 makes the observed regioselectivity understandable. Such regioselectivity is possible when both the diene and dienophile are nonsymmetrically substituted. Then dimerization can be of the *head-to-head* type with the formation of 1,2-disubstituted derivatives of cyclohexene or *head-to-tail* type if cyclohexene with substituents at positions 1 and 3 is formed. In ion-radical synthesis, head-to-tail dimerization is more typical. The charge distribution indicated in Scheme 7.20 explains this preference.

Stereospecificity manifests itself in the dimerization of a diene with a diene. The double bond that remains free may deviate from the ring formed (exo configuration) or approach it (endo configuration). Endo condensation is the predominant pathway in the case of ion-radical reactions (Scheme 7.21).

As seen, the charge distribution in the reactants dictates the head-to-tail pathway of the reaction. For the cation-radical, the positional selectivity at the C(1) atom is 100%, regioselectivity being 0%; whereas at the C(4) atom, the positional selectivity is 0% and regioselectivity is 100%. In other words, only the addition of the $D^{+\bullet}$-C(1) + D^{o}-C(4) type is observed (symbols D^{o} and $D^{+\bullet}$ refer to a neutral diene and diene in cation-radical form, respectively).

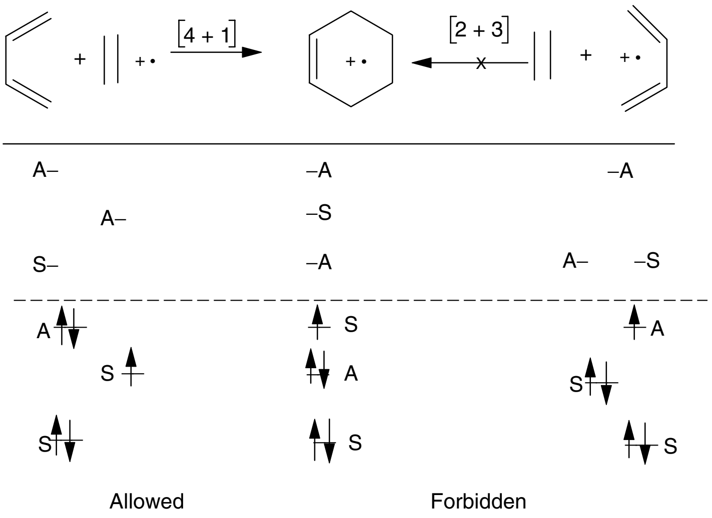
The cation-radical version of diene synthesis, in which the diene is in a strongly electron-deficient state, is characterized by an unusual high endoselectivity. In this case, endoselectivity is significantly higher than that of thermal or photochemical initiation of a neutral molecule (cf. Mlcoch and Steckhan 1987). As follows from the charge diagram depicted in Scheme 7.21, when a cation-radical and neutral molecule approach each other, not only the C(1)–C(6) and C(4)–C(5) interactions are bonding (indeed, these interactions result in cyclization), but C(2)–C(7) and C(3)–C(8) interactions are also bonding. As a result, the endo product is formed.

It is true that conventional diene condensations (without the cation-radical initiation) also proceed with the predominant formation of endo adducts. In the cation-radical version, endoselectivity increases sharply. This is quite understandable. The cation-radical acts as an independent particle, and the role of the suitable MO of the cation-radical turns out to be a determinant.

The publications of Bauld et al., which were reviewed earlier in Section 7.4.1, deal only with reactions in which a cation-radical (readymade) acted as a reactant. However, there can be cases where a cation-radical is formed in the course of donor–acceptor interaction between initially neutral molecules. Then the rigid or sharply enhanced selectivity of the reaction acquires diagnostic significance. For such cases, there is a general rule—condensation is permissible only for the (dienophile cation-radical + diene) pair and forbidden for the (dienophile + diene cation-radical) pair.

This rule can be understood from the orbital correlation diagram shown in Scheme 7.22, where the symbols S and A denote symmetric and antisymmetric orbitals, respectively (Bellville and Bauld 1982, Bauld et al. 1983).

The interaction between orbitals of equal symmetry is an indispensable condition of the condensation under consideration. As seen from Scheme 7.22, the condensation becomes possible only when the diene and dienophile supplies four electrons and one electron, respectively. Bauld et al. denote such interaction as [4 + 1]. If the diene and dienophile respectively supply three and two electrons (in the manner of [3 + 2] electrons), no cyclic adduct is formed.



SCHEME 7.22

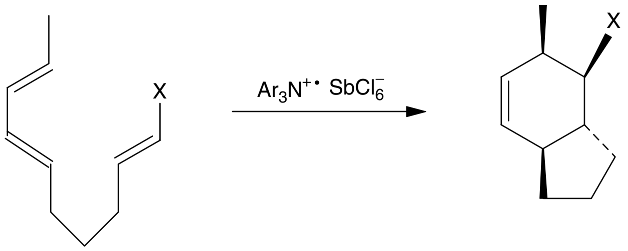
The simplest example is represented by pairs in which one-electron oxidation of a dienophile proceeds easier than that of a diene (Jia et al. 2003, Zhou et al. 2005). If cation-radicals of both the diene and dienophile can be formed on the action of a cation-radical initiator, some kind of separation operates. Each of these cation-radicals can exchange an electron with any participant in the reaction. However, since only the diene cation-radical is consumed, the equilibrium of the electron transfer is gradually shifted toward this particular cation-radical. The diene depicted in Scheme 7.22 enters the reaction in its *s*-cis form. If the diene cation-radical is in *s*-trans form, a cylobutane product forms (Reinolds et al. 1989, Botzem et al. 1998).

Naturally, the question arises as to whether the diene component really has to be in its *s*-cis form for the cation-radical Diels–Alder reaction. According to calculations by Hofmann and Schaefer 1999, the *s-trans*-butadiene is more stable than its *s*-cis isomer by 12 kJ · mol^{-1}, and for the cation-radicals, the trans preference is even somewhat pronounced (16 kJ · mol^{-1}).

However, the vinylcyclobutane cation-radical (when it forms) can rearrange to the cyclohexene cation-radical (Bauld and Yang 1999); the latter is more stable than the former by ca. 120 kJ · mol^{-1} (Haberl et al. 1999). Of course, such rearrangement is possible only when the vinyl group in the vinylcyclobutane structure has transformed from exo to endo configuration through rotation around the vinyl–cyclobutane bond. The rotation barrier is not high, therefore, "the cyclohexene cation-radical can be formed from ethylene and the *trans*-butadiene cation-radical as easily as from ethylene and *cis*-butadiene through a cation-radical vinylcyclobutane/cyclohexene rearrangement" (Hofmann and Schaefer 1999). It was shown experimentally that vinylcyclobutane can be converted into cyclohexene under electron-transfer conditions (Haberl et al. 1999).

It is now principally important to consider trienes with the general formula MeCH=CH−CH=CH−CH_2−CH_2−CH_2−CH=CHR. Such trienes contain moieties both of the diene and dienophile types within the framework of the same molecule. On initiation by the $Ar_3N^{+\bullet}$ cation-radical, cyclization takes place. Tetrahydroindanes are formed. The trienes of R=PhS, *p*-$MeOC_6H_4CH_2$, and H have been studied. The third triene, R=H, contains the dienophile fragment of lowered oxidizability; it is not cyclized at all. The diene synthesis proceeds in the cases of the first two trienes only (Harirchian and Bauld 1987; see Scheme 7.23).

As noted earlier, the reaction is initiated by an arylamine cation-radical, and dichloromethane is commonly used as a solvent. Recently, a simple but valuable technique has been elaborated for minimizing acid-catalyzed side reactions under aminiumyl salt conditions (Bauld et al. 2000). This technique consists of using a two-phase system of dichloromethane with water instead of only



X = 4-$MeOC_6H_4$ 83%
X = PhS 38%
Stereoselectivity 98–100%

SCHEME 7.23

dichloromethane. The use of water as a second phase was designed to remove any inorganic acid, which may have been present initially in the salt catalyst, and also to continue to extract these acids from the dichloromethane solution as they are formed. Since the salt catalyst is rather insoluble in water and typical cation-radical cycloaddition reactions are completed within 1–3 min or less, reaction efficiency is diminished only moderately by the presence of water. Under the two-phase conditions, the cyclopentadiene cycloaddition to *N*-vinylcarbazol is achieved although this dienophile is extremely prone to acid-catalyzed polymerization.

As noted in Section 1.3.2.1, one-electron oxidation causes deprotonation of cation-radicals. Because of this feature, attention must be given to the distinction between cation-radical and H-acid catalysis of cycloaddition. Bauld et al. elaborated a set of criteria, which allow one to differentiate these mechanisms from one another (Reinolds et al. 1987, Bauld et al. 1998b).

H-Acid Catalysis.

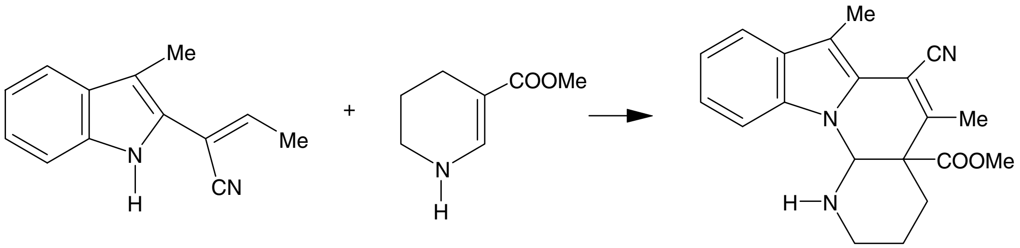
As a rule, H-acid catalysis lowers stereospecificity of the Diels-Alder reactions. Besides, kinetic parameters of these reactions correlates to the Hammett substituent constants. In the case of the cation-radical mechanism, correlation of kinetic parameters to the Hammett-Brown substituent constants gives the best accordance.

Cation-radical mechanism.

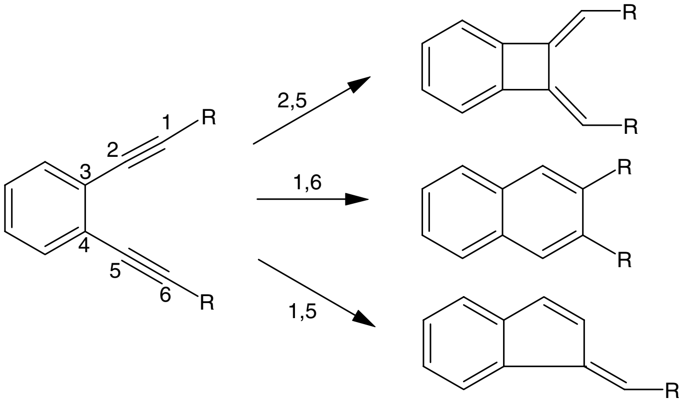
The sterically hindered base 2,6-bis(*tert*-butyl)pyridine does not inhibit cyclization; triarylamine retards this reaction; photosensibilized one-electron oxidation of a diene leads to the same products, which are formed in the presence of ammoniumyl salt. As shown, in majority of cases, only the cation-radical chain mechanism of the diene–diene cyclization is feasible (Bauld et al. 1987). Meanwhile, cyclodimerizations of 2,4-dimethylpenta-1,3-diene (Gassman and Singleton 1984) and 1,4-dimethylcyclohexa-1,3- or -1,4-diene (Davies et al. 1985) proceed through both mechanisms.

Guertler et al. (1996) described a wide range of cycloaddition reaction between 2-vinyl indoles acting as heterodienes and cyclic or acyclic enamines bearing acceptor groups in β positions. The reaction was induced by the formation of 2-vinylindole cation-radicals through anodic oxidation. The synthesis of 4a-carbomethoxy-6-cyano-5,7-dimethylindolo[1,2-a]-1,2,3,4,4a,12a-hexahydro-1,8-naphthyridine can serve as an example (Scheme 7.24).

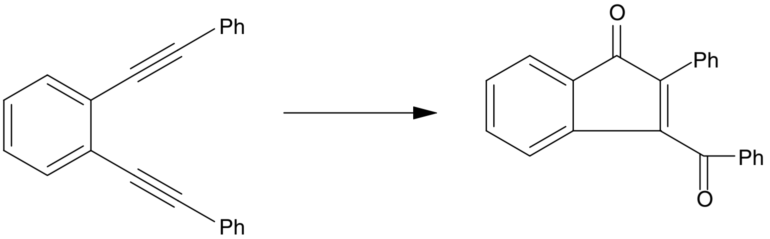
The known tendency of 2-vinylindole to homopolymerize is sufficiently low on the electrode surface. Therefore, an electrochemical initiation of the reaction under potentiostatic control is very favorable. The yield is high (90%), and the product formed is especially interesting because it incorporates the skeleton of the indole alkaloid goniomitine.



SCHEME 7.24



SCHEME 7.25



SCHEME 7.26

Intramolecular cyclization of *o*-diethynylbenzene gives us an opportunity to compare results of the thermal and cation-radical variants of the reaction. There are three possible modes of cyclization shown in Scheme 7.25.

Although the 1,6 cyclization takes place in the thermal process, the cation-radical initiation leads to the 1,5 cyclization (Ramkumar et al. 1996). Chemical oxidation of *o*-diethynylbenzene bearing two terminal phenyl groups by tris(*p*-bromophenyl)ammoniumyl hexachloroantimonate as the catalytic oxidizing agent *in the presence of oxygen* yields 3-benzoyl-2-phenylindenone in 70% yield (Scheme 7.26).

Scheme 7.26 reflects the final result of the reaction. The initial step of this reaction consists of one-electron oxidation of the substrate. The resulting cation-radical of *o*-diethynylbenzene transforms into a fulvenyl intermediate, which further reacts with the neutral substrate to yield fulvenyl

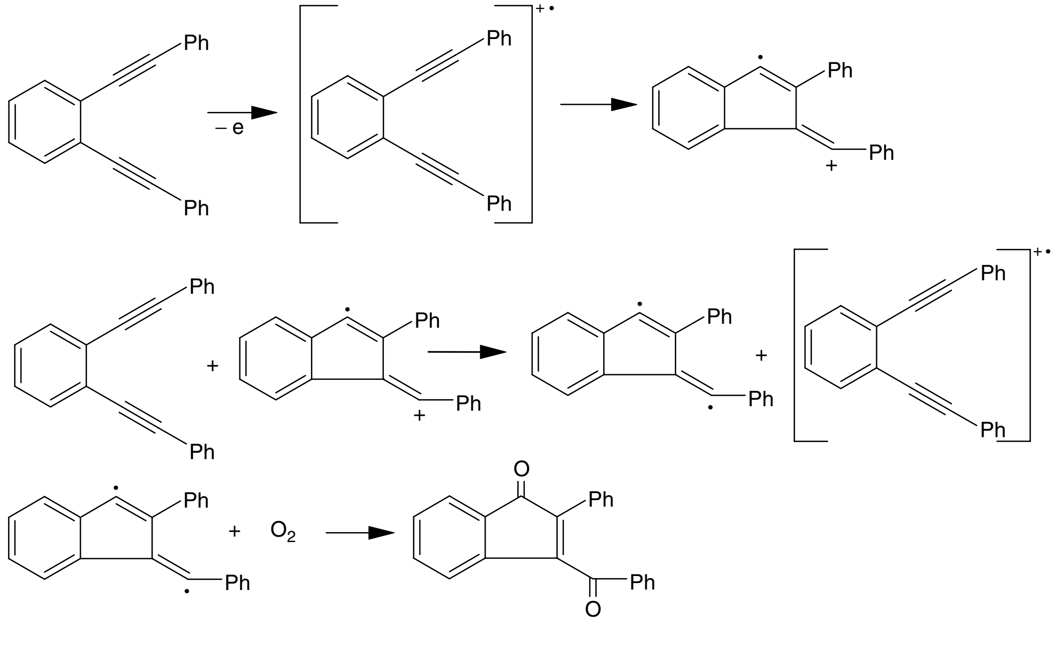
diradical and the substrate cation-radical. The latter is the chain carrier. The fulvenyl diradical adds oxygen and transforms into the final product. Scheme 7.27 represents this sequence.

According to the authors, the 1,5-cyclization mode of *o*-diethynylbenzene (see Scheme 7.25) is determined by electron state symmetry, which is different from that of the neutral molecule of *o*-diethynylbenzene (Ramkumar et al. 1996).

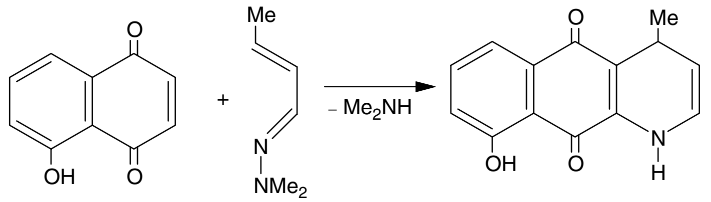
Sonochemically induced cation-radical intramolecular cyclization on action of an iodonium salt was also demonstrated (Arizawa et al. 2001). Being oxidized with phenyliodonium bis(trifluoroacetate), 1-(3-anisyl)-2-(1,3-cyclohexadien-2-yl) ethane formed the cation-radical and then 5′-methoxyspiro[cycloxehane-1,1′-indan]-2,6-dione. The yield of this final product was high enough.

Iodonium salts are at present receiving much attention because their reactivity is similar to those of heavy metal reagents. The results of the application of salts are similar to electrochemical oxidation. Added advantages, which render them synthetically more attractive are their low toxicity, ready availability, and easy handling. In contrast with the anodic version, the iodonium reactions are amendable to large-scale synthesis.

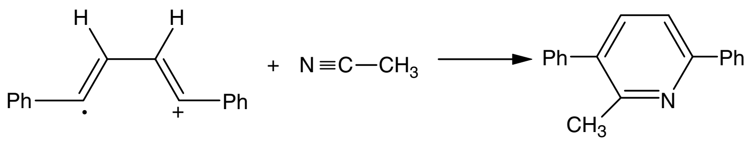
Turning from the intramolecular process to the intermolecular ones, we now extend our comparison of the thermal and cation-radical cyclizations. It is also interesting to take sonication into account as a route to initiate cyclizations. The reaction between 2-butenal *N*,*N*-dimethylhydrazone (a diene) and 5-hydroxy-1,4-naphthoquinone (a dienophile) gives such an opportunity. In toluene, at 20°C, the reaction follows as depicted in Scheme 7.28 (Nebois et al. 1996).



SCHEME 7.27



SCHEME 7.28



SCHEME 7.29

Without ion-radical initiation, the yield of the resulted product reaches 50% for 24 h. Practically the same yield can be achieved for the same time in the presence of tris(4-bromophenyl)ammoniumyl hexachloroantimonate and for only 6 h on sonication (Nebois et al. 1996). Sonication accelerates the rate-determining formation of the diene cation-radical. Of course, hydroxynaphthoquinone is strong enough as an electron-acceptor with respect to 2-butenal *N*,*N*-dimethylhydrazone. Therefore, the question remains whether sonication is more or less the general method for the initiation of ion-radical cycloaddition. A possible role of sonication in optimization of ion-radical reactions was considered in Section 5.2.5.

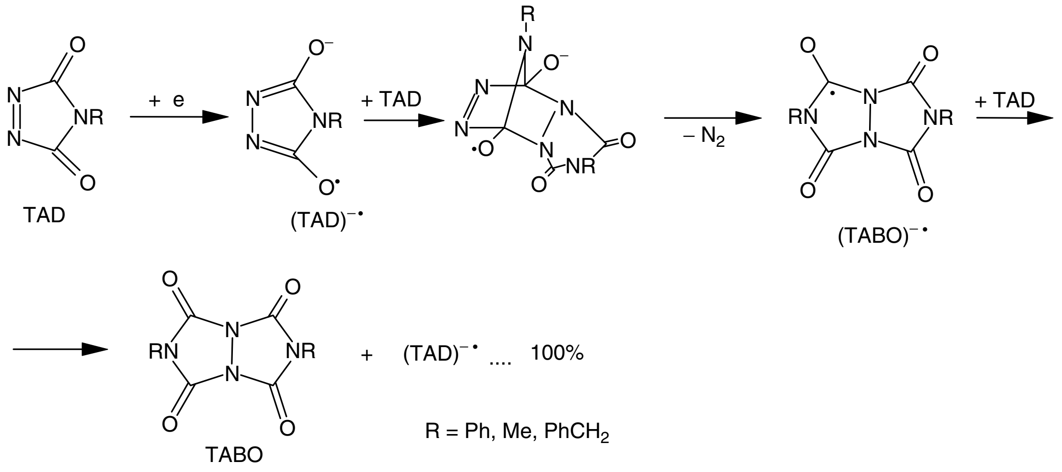
Additionally, we should mention the photoinitiated reaction between diphenylbutadiene cation-radical and AN (Mattes and Farid 1980; Scheme 7.29). De Lijser and Arnold (1998) have given a theoretical explanation to this reaction.

With respect to photoinitiation, generally, it is important to be very careful in one's choice of sensitizers. For example, attempts to initiate the cyclization of homobenzylic ethers failed if 1,4-dicyanobenzene was used as a sensitizer. Rapid regeneration of the starting material by back-electron transfer from the dicyanobenzene anion-radical to the substrate cation-radical was the cause of cyclization inefficiency. To slow this unproductive process, a mixture of *N*-methylquinolinium hexafluorophosphate (sensitizer), solid sodium acetate (buffer), and *tert*-butylbenzene (cosensitizer) in 1,2-dichloroethane was employed. This dramatically increased the efficiency of the reaction, providing cyclic product yields of more than 90% in only 20 min (Kumar and Floreancig 2001, Floreancig 2007).

7.4.2 Anion-Radical Ring Closure

As pointed out in Section 7.4.1, the head-to-head cyclodimerization is typical for phenylvinyl ether cation-radical (see Scheme 7.19). The anion-radical of phenylvinyl sulfone undergoes the same dimerization. The reaction is initiated electrochemically, develops according to the chain mechanism, and also leads to the trans-cyclic product (Bergamini et al. 2004).

As seen in Section 7.4.1, one-electron oxidation brings certain advantages to diene pericyclic reactions. One-electron reduction can also be advantageous for these processes. Let us first consider catalytic action of Lewis acids on Diels–Alder reactions involving carbonyl-containing dienophiles. Since the pioneering work of Yates and Eaton (1960), $AlCl_3$ has been known as an efficient catalyst for cycloaddition of α,β-unsaturated carbonyl compounds. However, due to its very high acidity, the catalyst initiates the significant polymerization of diene and dienophile. To prevent the polymerization, Fringuelli et al. (2006) used $AlCl_3$ (0.05 mmol) in the presence of THF (0.10 mmol) and not pure $AlCl_3$. Isoprene (a diene) and ethylacrylate (a carbonyl-containing dienophile) were contacted in 1.0:1.0 mmol ratio under solvent-free conditions. The mixture was stirred for 12 h at 30°C. The final reaction mixture was purified by silica gel column chromatography and the cycloadduct was isolated in 92% yield. The diene polymerization was avoided. The authors hypothesize that the formation of $AlCl_3 \cdot 2THF$ solvate lowers the acidic character of $AlCl_3$. The solvate is still able to activate ethylacrylate by oxygen complexation but is not able to react with isoprene to induce the polymerization. As shown by Fukuzumi et al., Lewis acids compose complexes with the ketyl (anion-radical) forms of carbonyl compounds. This assists one-electron transfer from a diene to a dienophile. The dienophile (ketyl) anion-radical undergoes cyclization. Lewis acids were arranged according to their ability of accelerating the electron transfer onto 1,4-benzoquinone from cobalt



SCHEME 7.30

tetraphenylporphyrin. Scandium tris[tetra(perfluorophenyl)borate] occurred to be the most active catalyst. It was $Sc[B(C_6F_5)_4]_3$, which accelerates cycloaddition of 1,4-benzoquinone or methyl vinyl ketone to 9,10-dimethylanthracene the most (Yuasa et al. 2003, Fukuzumi et al. 2002, 2005). In this catalyst, the scandium cation has the weakest nucleophilicity due to the huge volume of $[B(C_6F_5)_4]_3$ and electron withdrawing effect of fluorine within C_6F_5 moiety.

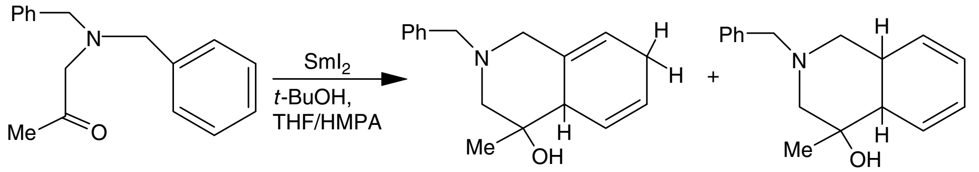
One-electron reduction of unsaturated α,δ-diketones may sometimes generate a diene structure and initiate condensation. Thus, triazoledions (TAD) pass into tetraazabicyclooctanetetraones (TABO). Naphthalene-sodium (ca. 1 mol%), sodium metal, or even sodium iodide efficiently catalyzes the reaction. Tetracyanoethyene and lead tetraacetate retard it. Consequently, the condensation has a chain character (Borhani and Greene 1986; Scheme 7.30).

Electroreductive one-electron initiation of cyclization was described for the series of *E*,*E*-1,7-dibenzoyl-1,6-heptadiene and its derivatives (Roh et al. 2002, Felton and Bauld 2004). In this case, the catalytic effect was also observed (the actual consumption of electricity was substantially less than theoretical). The same bis(enones) can also be cyclized on the action of the sodium salt of chrysene anion-radical in THF, but with no catalytic effect. Optimum yields were obtained only when 70–120 mol% of the *initiator* was used, relative to a substrate (Yang et al. 2004). The authors suggest that tight ion pairing of the sodium cation with the product anion-radical in THF (which is a somewhat nonpolar solvent) slows down the intermolecular electron transfer to the bis(enone) molecules. Such an electron transfer would be required for chain propagation.

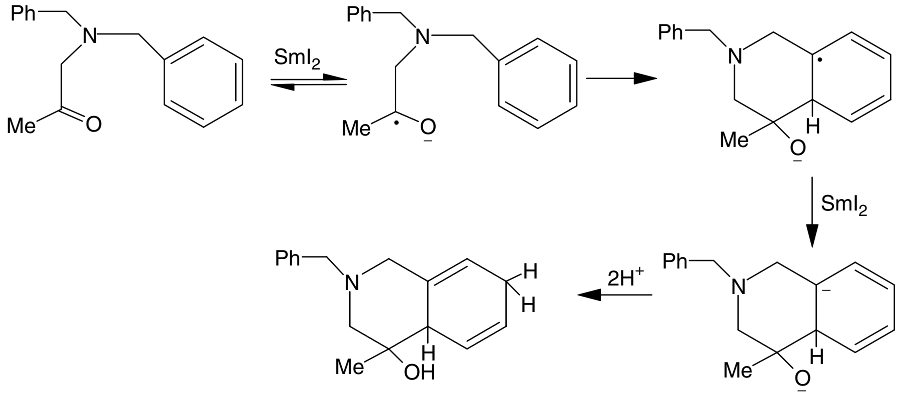
Several variants of SmI_2-induced cyclizations have attained synthetic importance owing to their high stereoselectivity (for reviews see Molander and Harris 1996, 1998). Samarium iodide is a very promising one-electron transfer reagent in organic chemistry (Section 1.7.13). Frequently, ketyl anion-radicals generated by electron transfer are the reactive species that undergoes intramolecular cyclization with the participation of a multiple bond at an appropriate distance. These ketyl anion-radicals can also attack an aryl moiety in an intramolecular fashion and, after a second electron transfer, lead to 1,4-cyclohexadiene derivatives. Let us take as an example the reaction of *N*,*N*-dibenzyl-substituted amino ketone, which produces an isomeric mixture of the isoquinoline derivatives, the total yield being 90% (Dinesh and Reissig 1999; Scheme 7.31).

Scheme 7.32 describes a possible mechanism of the reaction given by Scheme 7.31.

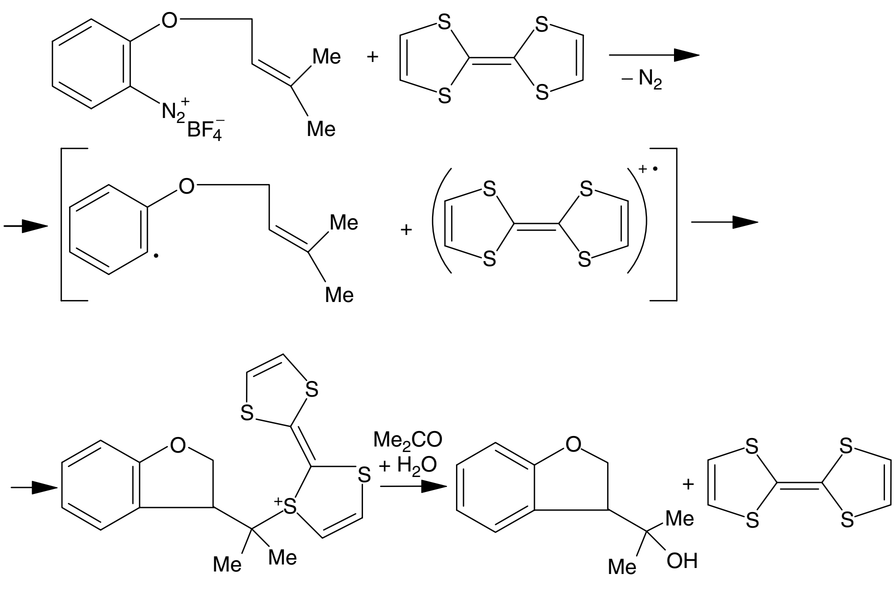
The first (reversible) electron transfer generates the ketyl anion-radical. The ketyl moiety then attacks the aryl group in the ortho position. The resulting cyclohexadienyl radical is reduced to a cyclohexadienyl anion by a second electron transfer, and the anion is finally protonated. HMPA as



SCHEME 7.31



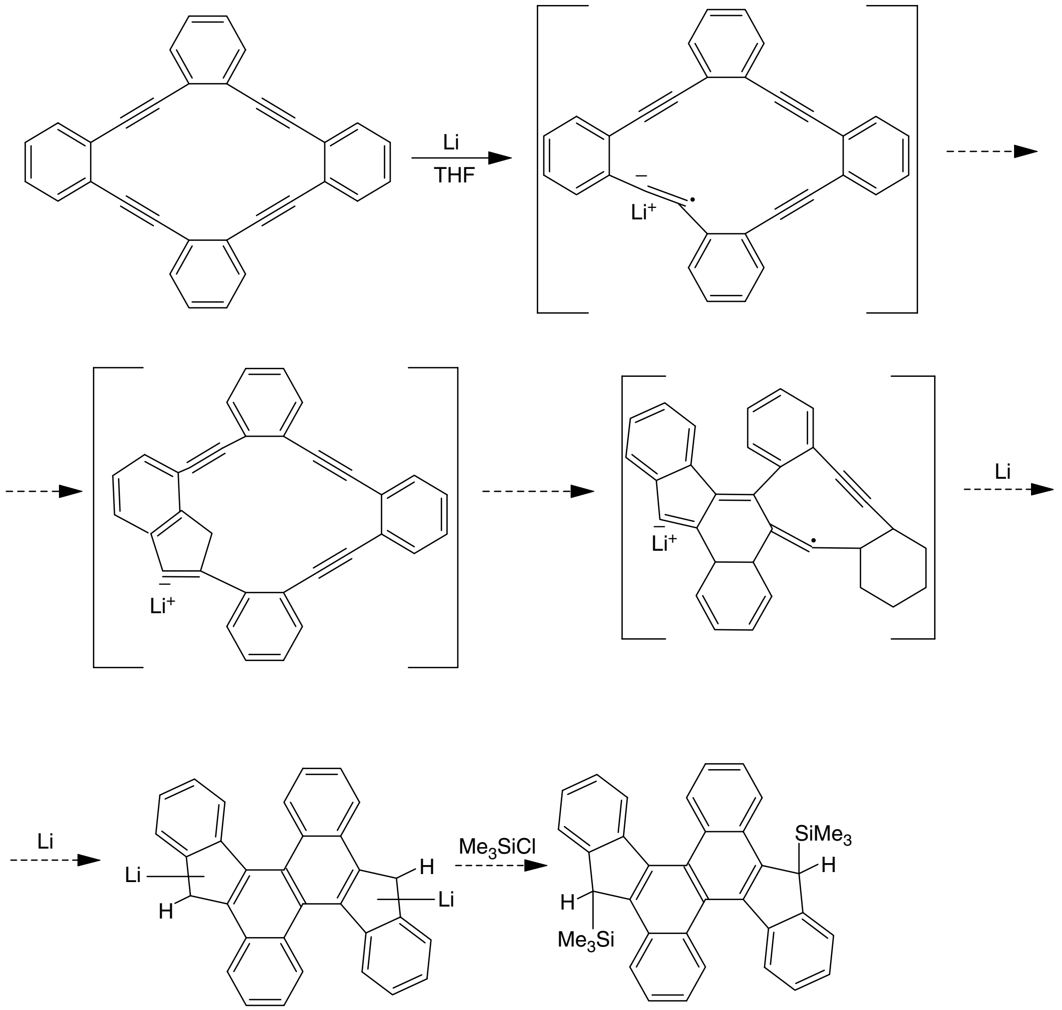
SCHEME 7.32



SCHEME 7.33

a cosolvent can be replaced with noncancerogenic *N*-methylpyrrolidone (Dinesh and Reissig 1999). This new reaction mode of samarium ketyls undoubtedly has a synthetic perspective.

Tetrathiafulvalene also provokes cyclizations. This can be seen from Scheme 7.33 (Lampard et al. 1993). In Scheme 7.33, the final cyclic alcohol is formed almost quantitatively and only 0.2 equivalent of tetrathiafulvalene is needed.

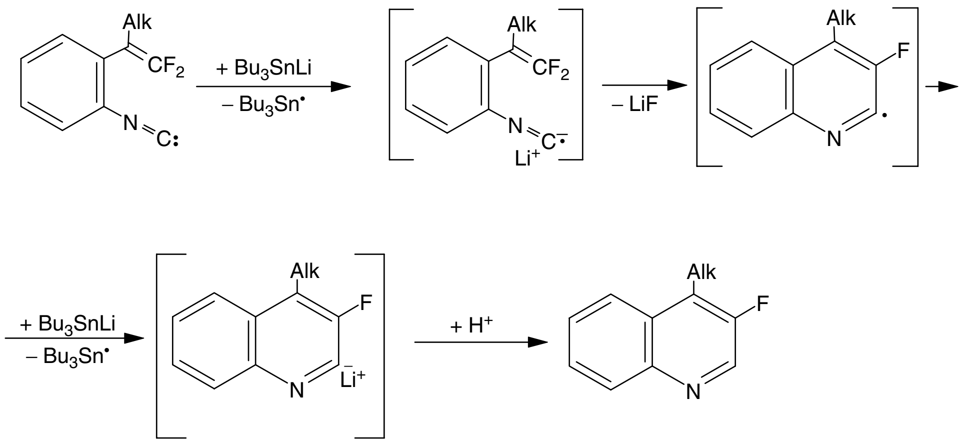


SCHEME 7.34

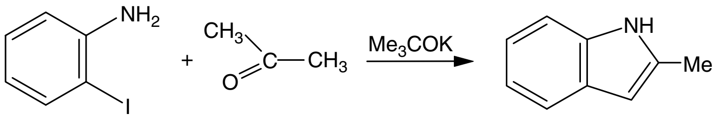
Another practically promising example of intermolecular anion-radical cyclization is a zipper reaction of cyclic *o*-ethynylbenzenes (Bradshaw et al. 1994; Scheme 7.34).

In Scheme 7.34, the final product, 9,8-bis(trimethylsilyl)diindeno[2,3-*g*:2′3′-*p*]chrysene (60% yield) has a helical geometry in the crystal state. The trimethylsilyl group is very reactive and can be involved in further reactions. Hence, this zipper cyclization offers a route to helical ribbon polymers from *o*-ethynylbenzene monomers. Such polymers are useful as conducting and nonlinear optical materials because of their π-electron conjugation, environmental stability, high mechanical strength, and enhanced threshold to laser damage. The most serious problem associated with such applications is that of poor solubility. However, helical aromatic ribbon polymers, in which the helical axes extend down the aromatic chains, usually have lower lattice energies and, therefore, higher solubilities than the planar system of comparable molecular weights. The reaction depicted in Scheme 7.34 foresees the possibility of extending the helical axes at the expense of the trimethylsilyl groups in the cyclic product.

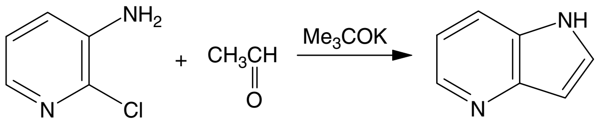
Ion-radical reactions also open convenient routes to fused benzoheterocycles as a result of intramolecular cyclization. The fused heterocycles are useful as compounds of potential physiological activity. Many of them are used as medications. Certainly, only those syntheses that do not change the functional groups needed to provide or enforce the curative effect, are of interest. At the same time, it is desirable to exclude acidic agents that lead to the splitting of the final heterocycles, which



SCHEME 7.35



SCHEME 7.36



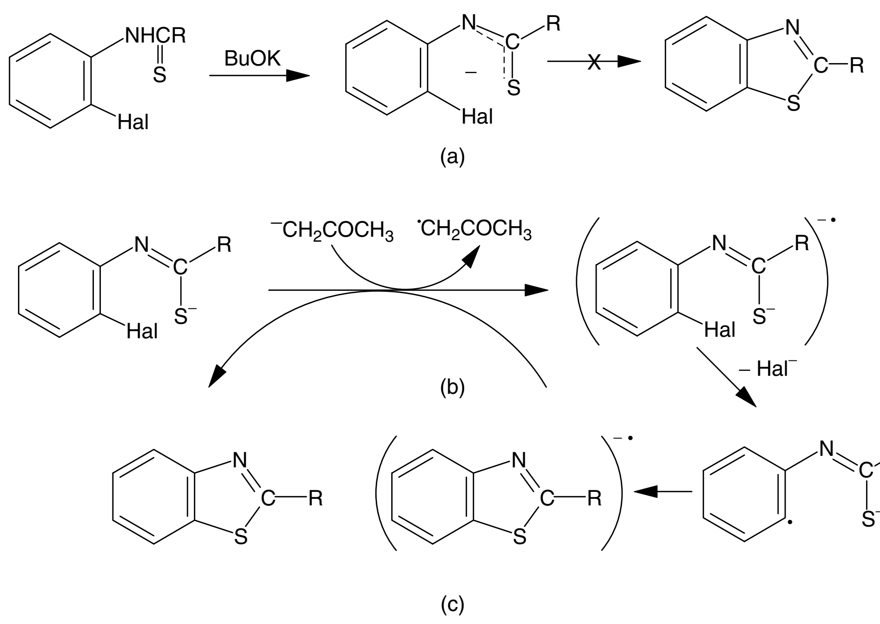
SCHEME 7.37

decrease yields or contaminate the desired products. Direct non-multi-step syntheses, which can proceed in mild conditions, are preferred. Many of these problems can be solved within the framework of ion-radical reactions.

Particularly, quinolines containing the fluorine substituent in position 3 are useful due to their lack of genotoxicity that is often observed in quinolines. This feature is principally important for medicinal and agricultural use (Kato et al. 1999). Ichikawa et al. (2004) synthesized 4-alkyl-3-fluoroquinolines by electron transfer from tributylstannyl lithium to *o*-isocyanato-β,β-difluorostyrene. The reaction includes reduction of the isocyano group in the substrate without affecting the difluoroalkene moiety. When the substrate is added to the reducer in THF (this order of mixing is important), the corresponding 3-fluoroquinoline is exclusively obtained in high yield. The authors presumed a mechanism as depicted in Scheme 7.35. According to this mechanism, isocyanides form anion-radicals on the action of tributylstannyl lithium. These anion-radicals are cyclized giving quinol-2-yl radicals and then are immediately transformed into carbanions in the form of lithium salts by the same reducer. Quenching the reaction with phosphate buffer (pH 7) leads to the final product 4-alkyl-3-fluoroquinoline.

Direct $S_{RN}1$(Ar) substitution reactions allow syntheses of isoquinolines (Beugelmans et al. 1984), indoles (Beugelmans and Roussi 1979, Barolo et al. 2003), and derivatives of benzothiazole (Boujlel et al. 1982), benzothiazine (Layman et al. 2005), or benzofurane (Vaillard et al. 2002) by "one-pot" syntheses. The photoinitiated synthesis of 2-methylindole is a representative example depicted in Scheme 7.36.

The one-pot synthesis of 4-azaindole is also initiated by photoirradiation; 3-amino-2-chloropyridine and acetaldehyde are the starting materials (Fontan et al. 1981; Scheme 7.37).



SCHEME 7.38

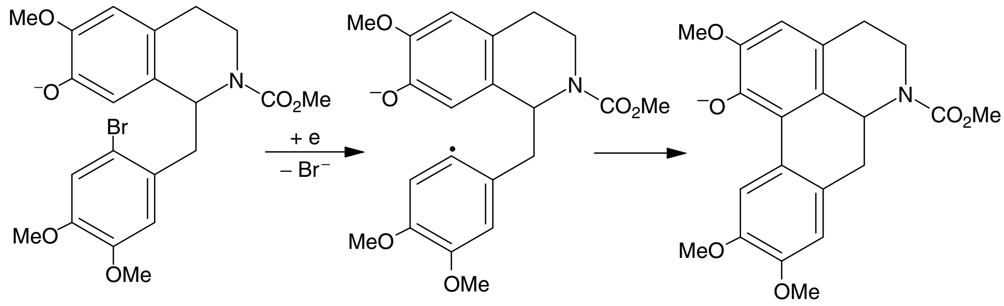
With conventional methods, the formation of indole derivatives from anilines proceeds at the expense of both unsubstituted ortho positions in the phenyl ring. This leads to undesirable by-products. Particularly, the formation of by-products takes place during Fischer's synthesis of benzoheterocycles. In the previously described ion-radical variant of the synthesis, only one indole isomer is formed—the isomer that corresponds strictly to the structure of the starting haloaniline.

The anion-radical mechanism for these syntheses is based on the following facts. The reactions require photo- or electrochemical initiation. Oxygen inhibits the reactions totally, even with photoirradiation. Indoles are formed from *o*-iodoaniline only; the meta isomer does not give rise to indole. Hence, the alternative aryne mechanism (cine-substitution) is not valid. What remains as a question is the validity of the ion-radical mechanism exclusively to the substitution of the acetonyl group for the halogen atom in *o*-haloareneamine or also for intramolecular condensation.

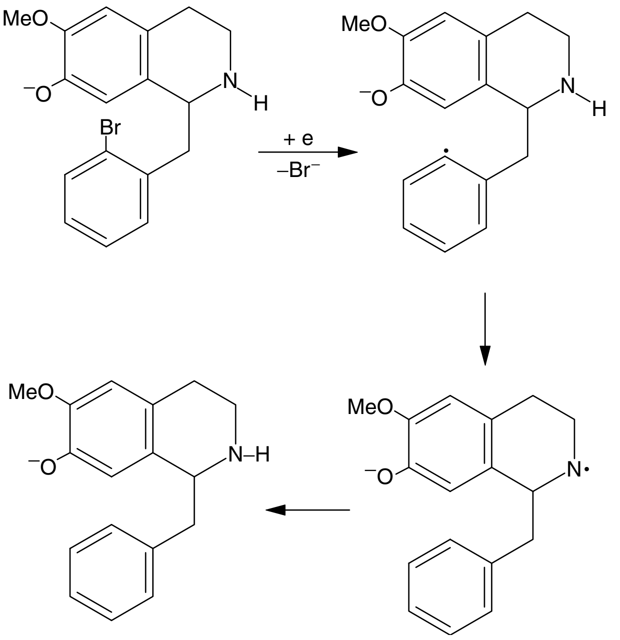
At this point, an unsuccessful attempt deserves to be mentioned. Creating a nonacidic procedure of benzothiazole syntheses, Bowman et al. (1982) tried to perform intramolecular cyclization according to reaction a, as depicted in Scheme 7.38.

However, reaction a in scheme 7.38 did not take place, irrespective of solvent polarity or the strength of the base. UV irradiation did not help either. Nevertheless, the cyclization appears to be successful in the presence of acetone (see reaction c in Scheme 7.38; Bowman et al. 1982). As usual, inhibitors stop this anion-radical reaction; 3-iodothiobenzanilide does not experience the cyclization. A principal point of this reaction consists of the understandable formation of the bond between the carbon-radical center and the negatively charged sulfur. Such a reaction is typical.

An important exception to this regularity is the cyclization of aromatic alkoxides containing aromatic radical moieties. In these cases, C–O bond formation is not observed, but C–C bond formation is achieved instead. As Galli and Gentili (1998) pointed out, this is primarily due to the unfavorable thermodynamic driving force for C–O bond formation compared to C–C bond formation. Thus, the photostimulated reaction depicted in Scheme 7.39 results in the formation of a six-membered carbocycle rather than an octa-membered oxa-heterocycle. The carbocycle is formed in 75% yield (Barolo et al. 2006). This product is a precursor to the thalicmidine biomolecule of the alkaloid group.



SCHEME 7.39



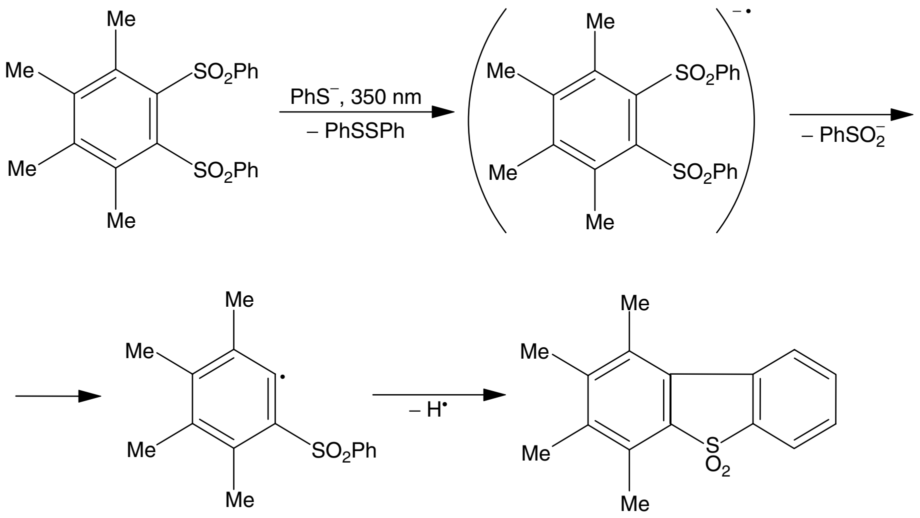
SCHEME 7.40

In the case of N–H analog of the starting material, cyclization is blocked by 1.5-hydrogen shift according to Scheme 7.40 (Barolo et al. 2006). Analogously, the anion-radical of bromoadamantane loses bromide and gives the adamantyl radical. This photoactivated radical also undergoes 1,5-hydrogen shift (Camps et al. 2001).

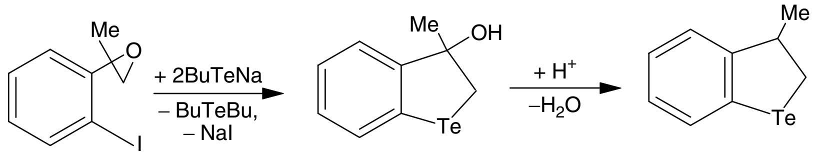
The phototransformation of 1,2-bis(phenylsulfonyl)-3,4,5,6-tetramethylbenzene into 2,3,4,5-tetramethyldibenzothiophene-*S*,*S*-dioxide on the action of arylthiolates should also be mentioned. The yield of dibenzothiophene-*S*,*S*-dioxide is more than 90%. The addition of *m*-dinitrobenzene prevents the cyclization. The reaction proceeds as shown in Scheme 7.41 (Novi et al. 1982).

As found by Engman et al. (1999), sodium alkyltelluroates are excellent reagents for the generation of aryl radicals from the corresponding iodides *in the dark*. Accordingly, 1-(2-iodophenyl)-1-methyloxirane reacts with two equivalents of sodium 1-butyltelluroate giving 2,3-dihydro-3-hydroxy-3-methylbenzo[*b*]tellurophene, which was isolated in 62% yield. The latter was readily converted into 2,3-dihydro-3-methylbenzo[*b*]tellurophene on treatment with a catalytic amount of *p*-toluenesulfonic acid (94% yield; Scheme 7.42).

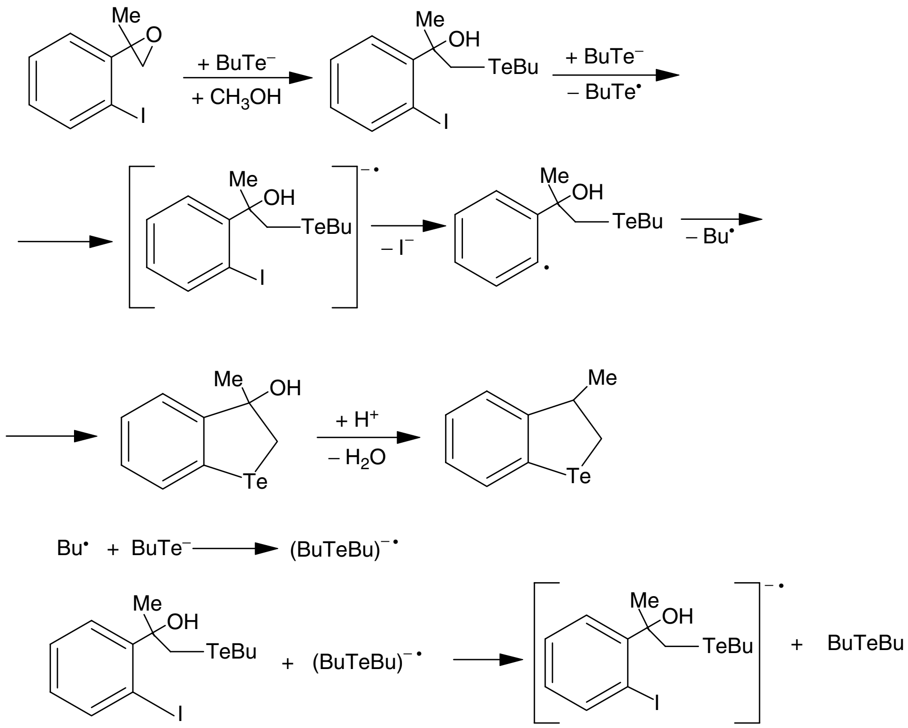
The reaction develops according to typical $S_{RN}1$ mechanism (see Scheme 7.43) and proceeds without photoirradiation.



SCHEME 7.41



SCHEME 7.42



SCHEME 7.43

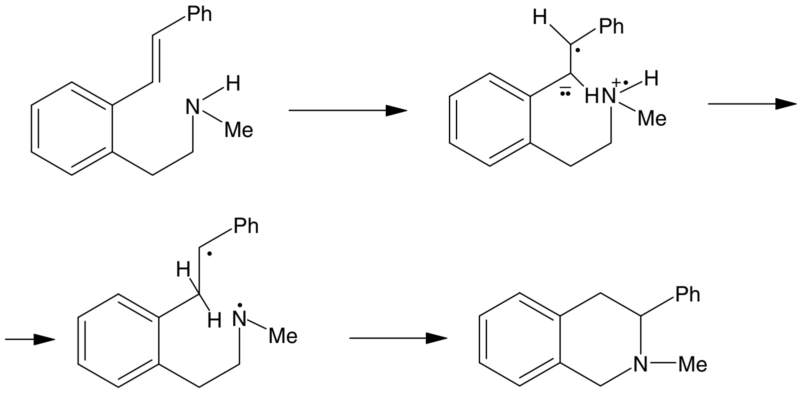
The practical significance of the reaction depicted in Scheme 7.43 consists of the development of novel antioxidants carrying chalcogen atoms. Divalent organochalcogen compounds react readily with many types of oxidants (peroxide, peroxyl radicals, peroxynitrite, singlet oxygen, and ozone). The tetravalent organylchalcogenides formed are reduced by many mild reductants. Therefore, compounds of this sort have the potential to act as catalytic antioxidants.

7.4.3 Ring Closure Involving Cation- and Anion-Radicals in Linked Molecular Systems

If a carbon chain separates an electron donor (D) and electron acceptor (A) sites in the same molecule, the exiplex-resembling state may originate on photoirradiation. Such an exiplex state represents some resonance hybrid of the electron-transfer configuration $[D^{+\bullet}–(CH_2)_n–A^{-\bullet\bullet}]$ mixed with the locally excited configuration $[D^*–(CH_2)_n–A]$ or $[D–(CH_2)_n–A^*]$.

The photolysis of donor–acceptor systems provides unique synthetic opportunities. Direct irradiation of the donor–acceptor systems, such as systems containing arene and amine components, leads to intramolecular electron transfer, that is, to amine cation-radical and arene anion-radical moieties. After generation, these moieties undergo cyclization reactions providing efficient synthetic routes to *N*-heterocycles with a variety of ring sizes. Thus, direct irradiation of secondary aminoethyl and aminopropyl stilbenes leads to benzazepines in improved yields (Hintz et al. 1996). As known, benzazepines are used in medicine as antidepressants. Scheme 7.44 illustrates ion-radical cyclization with the formation of benzazepine derivative (65% yield).

A representative example belongs to the systems linked topologically as in single crystals. The solid-state cycloaddition of bis(*N*-ethylimino)-1,4-dithiin to anthracene proceeds at the expense of the anthracene 9,10 positions. This is usual for anthracene cycloadditions. In single crystals, the reaction begins with the formation of an intermolecular (1:1) complex. The latter is formed as a result of electron (charge) transfer. The thermal heteromolecular solid-state condensation proceeds within the crystal. And this rare crystalline event is under topochemical control during the entire cycloaddition. As a result, a special crystalline modification of the cycloaddition product is formed, with crystal packing similar to that of the starting charge-transfer crystal. The modification is very different from that obtained from solution-phase crystallization. Such a single-phase transformation was readily monitored by x-ray crystallography at various phase-conversion stages. These temporal changes in crystallographic parameters are in correlation to the temperature-dependent (solid-state) kinetic data by ^{1}H NMR spectroscopy at various reaction times. Thus, an acceleration of the solid-state reaction over time was found. The acceleration results from a progressive lowering of the activation barrier for cycloaddition in a single crystal as it slowly and homogeneously converts from the reactant to the product crystal lattice (Kim et al. 2001).



SCHEME 7.44

7.5 RING OPENING

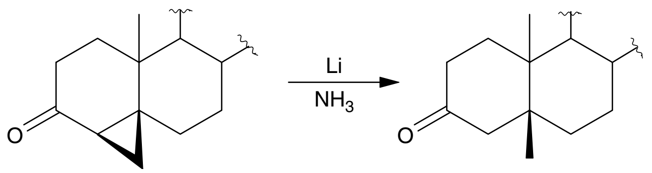
The three-membered ring in metal-ketyl anion-radicals can be readily opened. In steroid synthesis, this reaction is a classic procedure for introducing angular methyl groups (Dauben and Deviny 1966; Scheme 7.45).

The ring opening of 2-acylaziridines can be performed on the action of SmI_2 in THF–MeOH mixture. The final product—*N*-tosyl-β-aminoketone—is formed in 95% yield (Molander and Stengel 1995; Scheme 7.46).

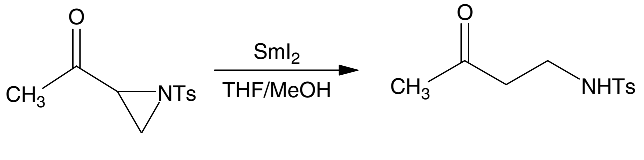
The reaction of 1,3-disubstituted bicyclo[2.1.0]pentanes with tris(4-bromophenyl)ammoniumyl hexachloroantimonate (the latter in catalytic amounts) leads to the corresponding cyclopentene after 1,2-hydrogen or 1,2-alkyl migration in the intermediary 1,3-cation-radicals (Adam and Sahin 1994; Scheme 7.47).

Adam and Heidenfelder (1998, 1999) analyzed regio- and stereoselectivity in the rearrangement of cyclopenta-1,3-diyl cation-radicals. The regioselectivity of the migration may be tuned through the electronic character of the substituents on the diyl sites, which was rationalized in terms of a single MO interaction diagram. The diastereoselectivity of the 1,2-shift is controlled by the steric factors in the intermediary 1,3-cation-radicals. The chemical one-electron oxidation of the initial fused structures with ammoniumyl salts has two advantages. On one hand, back-electron transfer to the cyclopentadiene-1,3-yl cation-radical is minimized, on the other, this reaction may be run on a preparative scale (Adam et al. 1995).

The ammoniumyl oxidant induces the quantitative conversion of a cage compound to the corresponding diene; the reaction proceeds for 1 min at room temperature (Hasegawa and Mukai 1985; Scheme 7.48).



SCHEME 7.45



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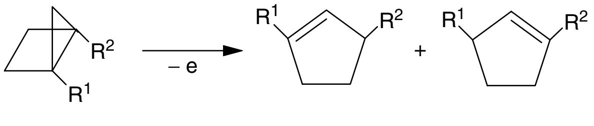

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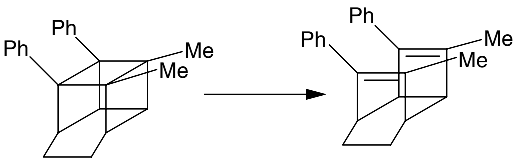
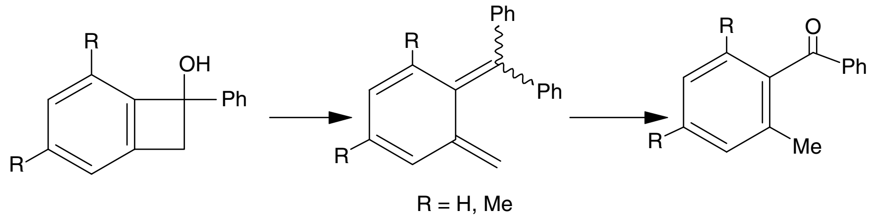


SCHEME 7.48



SCHEME 7.49

The addition of tetramethoxybenzene (a donor compound) retards the reaction. In the presence of this electron donor, the conversion degree is diminished up to 30%. Addition of alkylamines, such as triethylamine, diethylamine, or 1,4-diazabicyclo[2,2,2]octane, completely quenches the ring opening in this case. In contrast, triphenylamine does not quench the reaction (Hasegawa and Mukai 1985). These observations are consistent with the fact that alkylamine cation-radicals are less stable than arylamine cation-radicals (Chow et al. 1978). The ammoniumyl cation-radical converts triphenylamine into its cation-radical. The lifetime of the triphenylamine cation-radical is relatively long; therefore, this cation-radical can interact with the starting cage compound. This results in the conversion of the cage cation-radical into the cation-radical of the diene. One-electron reduction of this cation-radical by a neutral amine (triphenylamine or its tribromo analog) leads to the final diene compound. At this stage, triarylamine transforms into the corresponding cation-radical and returns to the catalytic cycle.

Takahashi et al. (1996) described another case of cation-radical cycloreversion. Benzocyclobutenols undergo ring opening induced by electron transfer to generate quinodimethide intermediates, which then tautomerize to benzophenones. The reaction proceeds on photoirradiation in the presence of tetracyanoanthracene ($\lambda > 350$ nm). Yields (based on NMR (proton) analyses) are quantitative (Scheme 7.49).

7.6 FRAGMENTATION

7.6.1 Selective Oxidation

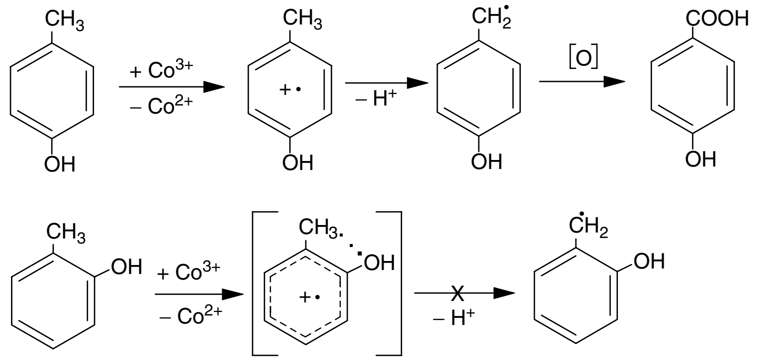
7.6.1.1 Selective Oxidation of Alkylbenzenes

Benzoic and hydroxybiphenyl carboxylic acids are widely used in the synthesis of drugs, biologically active compounds, and heat-resistant polymers. The known methods for preparation of aromatic hydroxy carboxylic acids include many stages, require not easily accessible starting compounds, and provide poor summary yields of the target products.

A method was proposed for the preparation of *p*-hydroxybenzoic acid by oxidation of *p*-cresol with atmospheric oxygen in an acetic acid–acetic anhydride mixture under catalysis of cobalt acetate, manganese(II) acetate, and sodium bromide (Litvintsev et al. 1994). This procedure ensures 60% yield of *p*-acetoxybenzoic acid and 100% conversion of the initial *p*-cresol.

In contrast to *p*-cresol, *o*-cresol does not undergo oxidation under these conditions. The same restriction is true in the case of 4-hydroxy-3,4′-dimethylbiphenyl—only one methyl group undergoes oxidation, the one in position 4′ (Koshel’ et al. 1997). The methyl group that is in position 3—ortho with respect to the hydroxy group—remains intact. Such inactivity is explained in terms of the cation-radical mechanism according to Scheme 7.50.

It is known that the oxidation of alkyl-substituted aromatic hydrocarbons in acetic acid on metal bromide catalysis follows the one-electron transfer mechanism (Sheldon and Kochi 1981). The rate-determining stage is the one-electron transfer from the substrate to the metal ion in the highest oxidation state (Digurov et al. 1986). As a result, an unstable cation-radical is formed that



SCHEME 7.50

loses a proton to give a more stable hydroxybenzyl radical. This is a typical proton-coupled electron transfer or concerted proton-electron transfer. The hydroxybenzyl radical reacts with oxygen, yielding at first an aldehyde and then carboxylic acid. Methyl hydrogen atoms in the cation-radical are more acidic than in the initial molecule (see Section 1.3.2.1). The loose proton of the methyl group in cation-radicals is capable of forming intramolecular hydrogen bond with the oxygen atom of the *o*-hydroxy group. This hydrogen bonding keeps the proton within the *fused* cycle, blocks the formation of *o*-hydroxybenzyl radical, and retards or prevents the consequent oxidation.

Such an explanation seems logical. A newly developed IR spectroscopic technique called *auto-ionization-detected IR* (ADIR) spectroscopy was applied for a study on hydroxy–alkyl interaction in *o*-cresol and *o*-ethyl phenol cation-radicals. The remarkable low-frequency shift of the O–H vibration was observed for these ortho derivatives only, and not for the meta- or para analogs (Fujii et al. 1998, Fujimaki et al. 2000). However, *ab initio* geometry optimization and topological electron density analysis led Vank et al. (2001) to the conclusion that there is "no evidence for this hydrogen bond" and the ADIR experimental data "should be explained without reference to a hydrogen bond" at all. According to Trindle (2000), the perturbative admixture of antibonding orbitals with the hydroxyl fragment orbital provides an effective rationale for the *o*-cresol cation-radical phenomenon. The future will hopefully uncover the truth; this is the way of science.

The selective oxygenation of ring-substituted toluenes to aromatic aldehydes and carboxylic acids has been one of the most important organic reactions in industrial chemistry because of the useful applications of aromatic aldehydes and carboxylates as key intermediates for the production of pharmaceuticals, dyes, pesticides, and perfumes. The known methods of aldehyde/carboxylate synthesis have been limited because of low yield and poor selectivity as well as the generation of copious amounts of inorganic waste. Ohkubo and Fukuzumi (2000) discovered a cation-radical method in which 100% selective oxidation of *p*-xylene to *p*-formyltoluene takes place. The reaction is initiated by photoinduced electron transfer from *p*-xylene to the singlet excited state of 10-methyl-9-phenylacridinium ion under visible light irradiation (in air). The yield of *p*-formyltoluene is quantitative. The reason for such high selectivity lies in the fact that the primary cation-radical readily loses a proton and transforms into *p*-methyl benzyl radical. This radical is trapped by the oxygen of air and eventually gives rise to *p*-formyltoluene.

$$[p\text{-}H_3CC_6H_4CH_3]^{+\bullet} \rightarrow H^+ + p\text{-}H_3CC_6H_4CH_2^\bullet$$

$$p\text{-}H_3CC_6H_4CH_2^\bullet + O_2 \rightarrow p\text{-}H_3CC_6H_4CH_2OO^\bullet$$

$$p\text{-}H_3CC_6H_4CH_2OO^\bullet + H^+ \rightarrow p\text{-}H_3CC_6H_4CH_2OOH \rightarrow H_2O + p\text{-}H_3CC_6H_4CHO$$

The liquid-phase oxidation of *p*-methylacetophenone is important from practical and methodological points of view and deserves a concise consideration. The reaction is performed in acetic acid with the cobalt acetate catalyst. As shown by Obukhova et al. (2002), the catalyst detaches an electron from the substrate. The latter forms the cation-radical, which can dissociate in the following two ways:

$$CH_3^{\bullet} + {}^{\bullet}CO–C_6H_4–CH_3 \leftarrow [CH_3CO–C_6H_4–CH_3]^{+\bullet} \rightarrow CH_3CO–C_6H_4–CH_2^{\bullet} + H^+$$

Under the conditions mentioned, the reaction exclusively leads to $CH_3CO–C_6H_4–COOH$, that is, it proceeds by maintaining the integrity of the acetyl group. Two factors in concordance make such a regioselectivity possible. First, spin delocalization in the acetylbenzyl radical takes place more effectively than that in the methylphenyl carbonyl radical. In other words, the acetylbenzyl radical forms preferentially. Second, solvation of the separating proton is more favorable than that of the methyl radical because the proton size is smaller. The kinetic data by Obukhova et al. (2002) are in full agreement with the mechanism operating in the formation of *p*-acetylbenzoic acid as the sole final product of the reaction.

7.6.1.2 Selective Oxidation of Dimethylimidazole

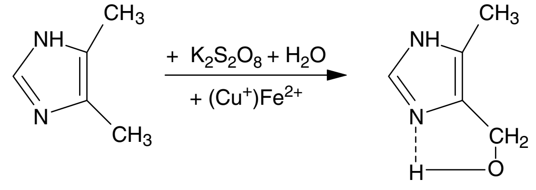
Methylated *aromatic* heterocycles ($HetCH_3$) form cation-radicals that are typical π acids and expel a proton. Methylene radicals are formed. These radicals give rise to the corresponding carbocations if an oxidant was taken in excess. Nucleophiles attack the ions, completing the reaction. If water is the reaction medium (the hydroxyl anion is a nucleophile), an alcohol is formed. The alcohol rapidly transforms into an aldehyde on the action of the same oxidant.

$$HetCH_3 - e \rightarrow HetCH_3^{+\bullet} \rightarrow HetCH_2^{\bullet} - e \rightarrow HetCH_2^+$$

$$HetCH_2^+ + OH^- \rightarrow HetCH_2OH \rightarrow HetCHO$$

During oxidation of 4,5-dimethylimidazol by peroxydisulfate in water, the reaction is stopped just at the alcohol-formation step. The alcohol is stabilized due to intramolecular hydrogen bonding. This keeps the alcohol safe from further oxidation (Citterio and Minisci 1982; Scheme 7.51).

The final product, 4-hydroxymethyl-5-methylmidazol, is a key intermediate in the industrial synthesis of cimetidine—the effective antiulcer drug. The cation-radical route to the methylimidazol carbinol is practically waste-free with respect to the organic substance. The desired product is formed in 70% yield, and the starting material returns for 30% yield (Citterio and Minisci 1982). It is worth noting that the starting material is easily obtained from cheap methylethyl ketone. Other methods of carbinol preparation are less effective. Hydroxymethylation of 4-methylimidazole is less selective, and reduction of 4-methylimidazol-5-carboxyethylate is characterized with lowered yields of the target product.



SCHEME 7.51

7.6.2 Cation-Radical Route to Group Deprotection

The protection of certain functional group and deprotection of the protected derivatives constitute important processes in the synthetic organic chemistry of polyfunctional molecules, including the total synthesis of natural products (Jarowicki and Kocienski 1995). Examples demonstrating some serious improvements to the conventional methods for group deprotection are as follows.

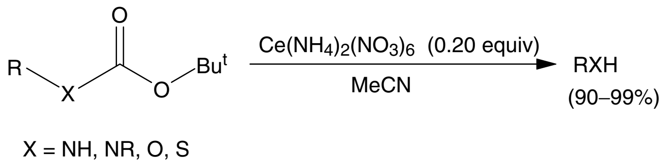
7.6.2.1 Removal of Butoxycarbonyl Protective Group

The *tert*-butoxycarbonyl (BOC) group is often used for the protection of amino, hydroxy, and sulfhydryl groups. This kind of protection is usual in the chemistry of amino acids and peptide synthesis.

Reagents that remove the BOC group include hydrochloric acid in ethyl acetate (Stahl et al. 1978), sulfuric acid in dioxan (Houghton et al. 1986), anhydrous hydrogen fluoride (Yamashiro et al. 1972), boron trifluoride etherate in acetic acid (Schnabel et al. 1971), trimethylsylil triflate (Schmidt et al. 1987), trimethylsilyl perchlorate (Vorbrueggen and Krolikiewicz 1975), and, most frequently, trifluoroacetic acid (see Kocienski 2003). Deprotection of the BOC group under neutral conditions has not been described till now, yet it is highly desirable. Now it has been found that *tert*-butoxycarbonyl protecting group for amines, alcohols, or thiols is removed efficiently (90–99% yield) by using 0.2 equivalent of cerium ammonium nitrate in AN at 80°C (Hwu et al. 1996; Scheme 7.52).

The proposed mechanism includes transformation of the carbonyl group into the cation-radical state while reduction of Ce(IV) to Ce(III) takes place. The cation-radical then undergoes fragmentation to give the *tert*-butyl cation and carboxylic radical. Regeneration of Ce(IV) from Ce(III) during reduction of the carboxylic radical to the carboxylate ion allows the use of cerium ammonium nitrate in catalytic amounts for the entire deprotecting process. Finally, extrusion of CO_2 from the carboxylate ion followed by protonation gives the free amine (Scheme 7.53).

Hence, the method has been worked out to remove the *tert*-butoxycarbonyl group that protects amines, alcohols, or thiols under neutral conditions rather than the conventional strongly acidic



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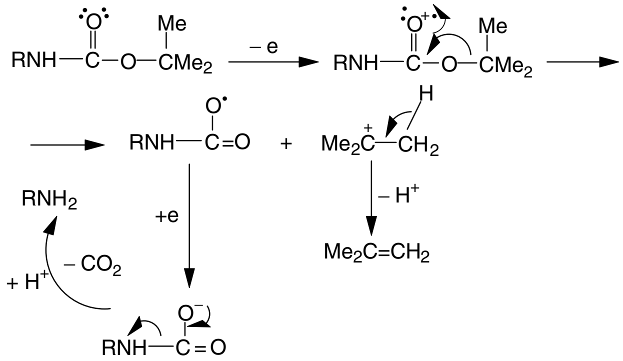


SCHEME 7.53

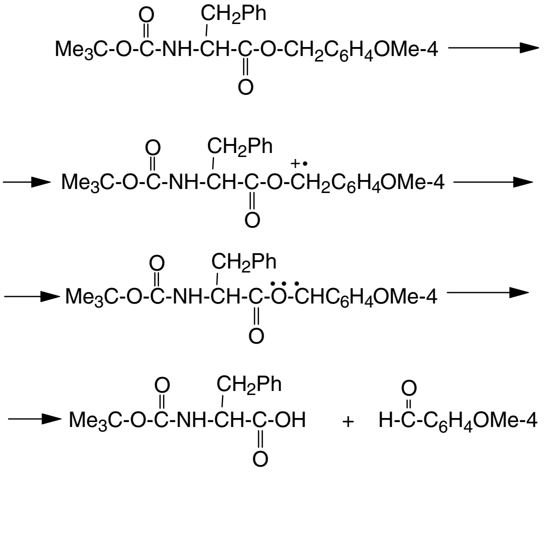
conditions. It was reported that high-yield deprotection can be achieved by using catalytic amounts of ceric ammonium nitrate in refluxing AN. The data are given on a variety of the BOC-protected substrates, including the ones containing acid-labile groups.

The catalytic effects and versatility of cerium(IV) ammonium nitrate as a single-electron oxidant were recently reviewed (Nair and Deepthi 2007, Maulide et al. 2007). However, it should be kept in mind that this oxidative reagent is very powerful and some sensitive functions are not compatible with it. Particularly, some amines are at least as easily oxidizable as the starting molecule bearing the protected group. Anodic oxidation was proposed as a useful alternative (De Lamo Martin et al. 2005).

7.6.2.2 Removal of Methoxybenzyl Protective Group

The methoxybenzyl group is often employed for the protection of the carboxyl function. Let us consider the completely protected phenylalanine as an example. In complicated syntheses of natural or biologically active compounds, it is very important to remove the protection of one functional group and maintain the protection of another group in a polyfunctional molecule. Such a molecule is a phenylalanine derivative, with the NH_2 and COOH functions protected by *tert*-butoxycarbonyl and *p*-methoxybenzyl groups, respectively. Both protective groups are saponified in acid media. Therefore, usual methods are not applicable for selective deprotection. However, these two functions differ in their electron-donor capabilities. Therefore, single-electron oxidation by tris(4-bromophenyl)ammoniumyl hexachloroantimonate leads to the formation of a cation-radical with the spin-positive density centered on the benzylic fragment. The one-electron oxidized benzylic group expels its proton. A radical center emerges, and this center is adjacent to the oxygen atom bearing an electron pair. This electron pair and the unpaired electron of $CH_2^{\bullet}$ group form a three-electron bond, and the oxygen–benzylic spin localization becomes even more pronounced. It is O–CH_2 bond that is eventually split. The breakdown proceeds with strict selectivity; the *N*-acylated phenylalanine is formed with more than 90% yield. Scheme 7.54 illustrates the transformations described (Dapperheld and Steckhan 1982).

Because the compared protective groups in phenylalanine also differ in their electron acceptor activity, one can expect that anion-radical generation would result in the selective removal of amine protection. This assumption is supported by the ESR studies of some peptide cation-radicals (Lin et al. 1998). For instance, neat histone (a protein from cell nuclei) gives an anion-radical in which the unpaired electron is localized at the amidocarbonyl function.



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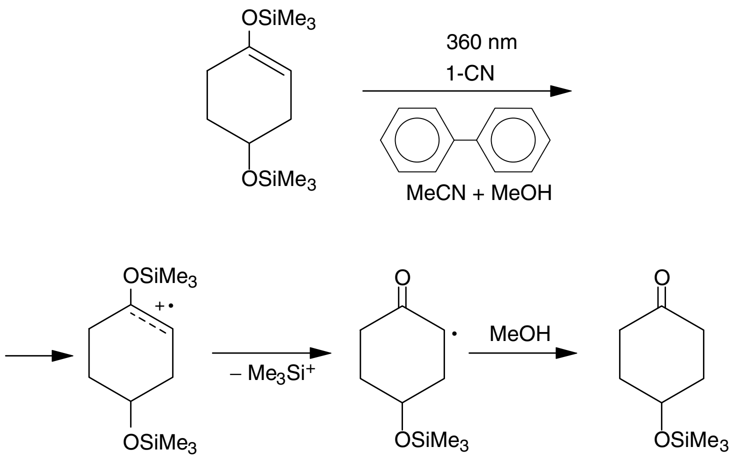


SCHEME 7.55

7.6.2.3 Removal of Trimethylsilyl Protective Group

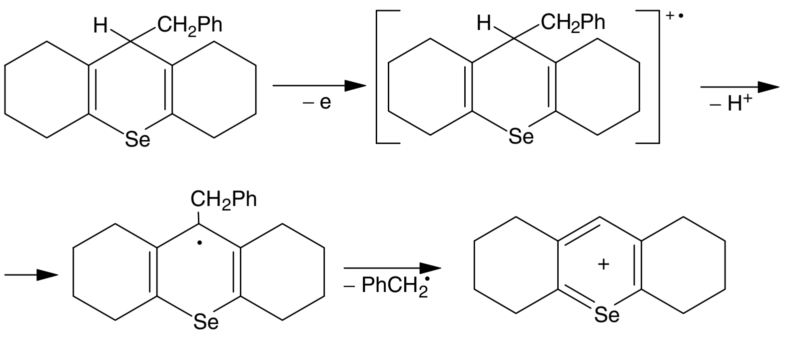
The trimethylsilyl moiety is now widely used as a protecting group for alcohols (through the formation of trimethylsilyl ethers) or aldehydes and ketones (through the formation of trimethylsilyl enol ethers). The trimethylsilyl-protecting group has routinely been removed with fluoride ion, acids, or bases. Unfortunately, these reagents offer little in terms of selectivity between trimethylsilyl ethers and trimethylsilyl enol ethers. Gassman and Bottorff (1988) proposed a selective method to cleave the trimethylsilyl enol ether group in the presence of the trimethylsilyl ethereal moiety. The method is elegant, although it is presently not accepted in laboratory practice. The initial step of this reaction consists of photoinduced one-electron oxidation of the trimethylsilyl enol ethereal moiety. The trimethylsilyl ethereal group remains intact. In the protocol, diprotected 4-hydroxycyclohexanone was irradiated in the presence of biphenyl and 1-cyanonaphthalene (1-CN) for 5 h (300 nm, 40:60 methanol/AN; Scheme 7.55).

The half-deprotected product was obtained in 65% yield. Of course, such a yield is insufficient from a synthetic point of view, the photovariant of the redox reaction is not simple instrumentally, and the duration of the reaction (5 h) is too long. Nevertheless, this approach is promising, and deserves attention and development. Thus, the photochemical method proved to be successful in the removal of protecting groups based on covalently linked donor–acceptor systems (Lee and Falvey 2000).

An economical, practical, and environmentally acceptable procedure was elaborated for oxidative deprotection of trimethylsilyl ethers to their corresponding carbonyl compounds. The reaction proceeded in a solventless system, within a short period of time, and yields were good. On irradiation in a conventional microwave for 30 s, trimethylsilyl ether of benzyl alcohol in the presence of montmorilonite K10 and finely grounded $Fe(NO_3)_3 \cdot 9H_2O$ gave rise to benzaldehyde in 95% yield. The applicability of this method was tested with several aromatic, alicyclic, and aliphatic trimethylsilyl ethers. Duration did not exceed 1 min, and yields were not lower than 80% (Mojtahedi et al. 1999).

7.6.3 Scission of Carbon–Carbon Bonds

In most cases, the higher the one-electron reduction/oxidation potential of the molecule, the higher is the energy level of the resulting anion/cation-radical and lower is its bond dissociation energy. This self-obvious statement is useful in terms of the first prediction of the ion-radical reactivity. Besides the potential value, the substituent nature is also a sign of bond dissociation to occur. Namely, substituents can exert serious steric hindrance in the reactant or they can especially stabilize fragments



SCHEME 7.56

resulting after bond scission. Thermodynamic and kinetic aspects of bond cleavage are unified according to a review by Schmittel and Ghorai (2001). Here, some representative examples are considered from the synthetic point of view.

The so-called mesolytic fragmentation processes are more commonly activated by the removal of an electron, initially leading to the formation of cation-radicals. Then the carbon–carbon bond scission occurs—the bonds that are quite strong in uncharged substrates. There are also few examples of mesolytic fragmentation following the attachment of an electron, that is, fragmentation of anion-radicals. One such example belongs to the bisanthrone derivative, 1,8,1′,8′-tetrahydroxy-9,9′-bis(10*H*-anthracenone; Czerwinska et al. 2006). On one-electron reduction, this bisanthrone gives rise to an anthranyl anion (the 9-enolate of 1,8,9-trihydroxyanthracene) and the corresponding radical (9-hydroxyl radical of 1,8,9-trihydroxyanthracene).

Scheme 7.56 represents another example of the cleavage of a carbon–carbon bond. The cation-radical of 9-benzyl-*sym*-nonahydro-10-selenaanthracene expels a proton and then the benzyl radical (trapped) giving *sym*-octahydro-10-selenaanthracene trifluoroacetate in a quantitative yield (Blinokhvatov et al. 1991). The formation of the benzyl radical and aromatization of the central hetero ring of the cation-radical facilitate the development of the reaction.

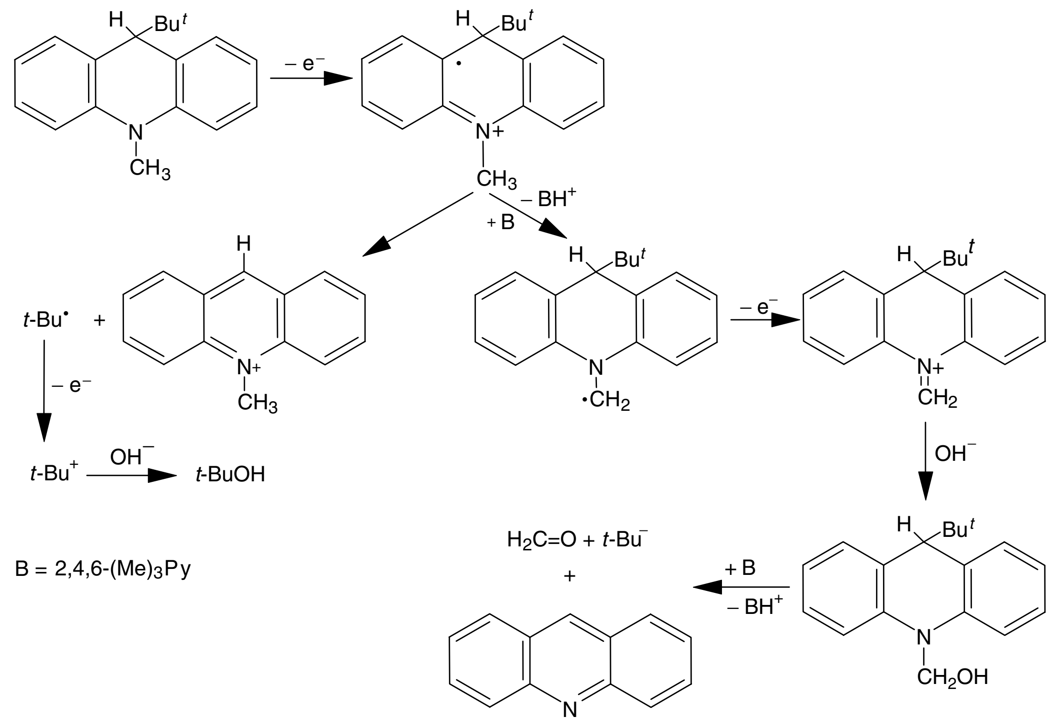
Another, even more influential, example is double fragmentation in the cation-radical of 9-*tert*-butyl-*N*-methylacridan shown in Scheme 7.57. The cation-radical was generated electrochemically or photochemically (Anne et al. 1998). In acidic or weakly basic media, the *tert*-butyl radical is cleaved, with the formation of methylacridinium cation. This direction is depicted in the left-hand side of Scheme 7.57, where 2,4,6-trimethylpyridine is marked as a base. If a strong base is used, the direction that leads to acridine, formaldehyde, and *tert*-butyl carbanion is chosen. This direction is depicted in the right-hand side of the scheme. The origin of such a dual behavior resides in prior deprotonation of the methyl group borne by the nitrogen atom that outruns the usual deprotonation at the 9-carbon atom. The deprotonation at the 9-carbon is slowed by steric hindrance due to the presence of the *tert*-butyl group. This steric hindrance effect on the cation-radical deprotonation was noted in Section 1.3.2.1. This example is important because carbon bond fragmentations occur at the first stages of the cation-radical evolutions in case of tert-butylated analogs of nicotinamide adenine dinucleotide (NADH; Fukuzumi et al. 1993).

Examples of cation-radical deprotonation–fragmentation of alcohols also deserve a separate consideration. Hammerum and Audier (1988) described the following reactions:

$$PhCH_2CH_2OH \rightarrow (PhCH_2CH_2OH)^{+\bullet} \rightarrow H^+ + PhCH_2^{\bullet} + CH_2{=}O$$

or

$$Me_3CCH_2OH \rightarrow (Me_3CCH_2OH)^{+\bullet} \rightarrow H^+ + Me_3CH_2^{\bullet} + CH_2{=}O$$



SCHEME 7.57

The carboradicals formed act as effective alkylating agents. The driving forces behind these reactions consist of the formation of rather stable radicals ($PhCH_2^•$ and $Me_3CH_2^•$) after deprotonation. Proton is also a stable particle. The formation of formaldehyde also helps to drive the reactions.

In this connection, it is interesting to compare the cation-radicals of 1,2-diphenyl- and 1,1,2,2-tetraphenylethanes in their ability to expel a proton or to cleave the exocyclic C–C bond. The former cation-radical preferentially reacts by deprotonation (Camaioni and Franz 1984, Baciocchi et al. 1986). The C–C bond strength of 121.5 kJ · mol^{-1} in 1,2-diphenylethane cation-radical is too high. At the same time, the C–C scission induced by electron transfer is only feasible if the strength of this bond is lesser than 42 kJ · mol^{-1}. In the case of 1,1,2,2-tetraphenylethane cation-radical, this magnitude is equal to 38 kJ · mol^{-1} only, and the C–C scission indeed takes place (Arnold and Lamont 1989).

$$(Ph_2CH{-}CHPh_2)^{+\bullet} \rightarrow Ph_2CH^\bullet + Ph_2CH^+$$

On adding the hydroxyl substituent to the CH_2CH_2 unit, the barrier for C–C scission is lowered because of more favorable thermodynamics (Albini and Spreti 1987, Barton et al. 1996). However, the hydroxyl substituent becomes effective only after its deprotonation. Cation-radicals of 2-, 3-, and 4-arylalkanols, all of them, undergo C(1)–H deprotonation at pH 4. At pH 10, they display a different behavior. The 2-(4-methoxybenzene)ethanol cation-radical experiences C(2)–C(1) scission, resulting in the formation of formaldehyde and 4-methoxybenzyl radical; the 3-(4-methoxybenzene)propanol cation-radical gives rise to 3-(4-methoxybenzene) propanal; the 2-(4-methoxybenzene)butanol cation-radical behaves as the C_α–H acid both in acidic and basic solutions (Baciocchi et al. 1996, 1999a).

In the 1-arylalkanol cation-radicals, only C(1)–H deprotonation takes place at pH 4; at pH 10, C(1)–C(2) bond cleavage proceeds. Replacement of an 1-OH group by OMe has a very slight effect on the decay rate when the cation-radical undergoes deprotonation, but has a very large and negative effect in the case of C(1)–C(2) bond cleavage (Baciocchi et al. 1999b). It is suggested that

the hydrogen bonding of 1-OH group with water (the solvent) stabilizes the transition state of the C(1)–C(2) bond fragmentation reaction but not that of the deprotonation process. Of course, other factors could also contribute to this phenomenon.

The unpaired electron and positive charge in arylalkane cation-radicals are localized essentially on the aromatic rings. This suggests that carbon–carbon bonds within the alkyl chain are slightly affected as a result of arylalkane one-electron oxidation. What really happens in the course of the C–C bond cleavage? How is the C–C bond activated in the cation-radicals? Chanon et al. (1990) as well as Takahashi and Kikuchi (1991), pointed out that the transformation of a neutral arylalkane into a cation-radical does evoke some bond elongation in the alkyl fragment. The degree of this elongation depends on the nature of alkyl chain. When elongation is serious, the cation-radical transforms from an *aromatic* to an *alkane* cation-radical. The unpaired electron density sharply decreases in the phenyl ring and increases in the alkyl framework. The latter becomes ready for cleavage.

7.6.4 Synthon-Influential Bond Scission

The generation of active radicals as a result of bond breakage makes cation-radicals useful as synthons. For example, arylsulfenamide cation-radicals may be used as sources of sulfenyl radicals. The reaction of 4′-nitrobenzenesulfenanilide with Lewis acids, such as BF_3 and $AlCl_3$, leads to the formation of sulfenamide cation-radical. The latter appears to be an active sulfenyl transfer species. In the presence of anisol, ethenes, or ethynes, it gives phenylthiyl derivatives (Benati et al. 1990, Grossi and Montevecchi 1993).

Cleavage of carbon–nitrogen bonds is also important in synthetic and, sometimes, biomedical ion-radical chemistry. Thus, triazenes are regarded as carcinogenic compounds. Speiser and Stahl (1992) showed that the benzenediazene cation-radicals easily eliminate –N=N– fragment together with an unpaired electron.

$$(p\text{-}Me_2N\text{–}C_6H_4N\text{=}N\text{–}NMe_2)^{+\bullet} \rightarrow N_2 + (p\text{-}Me_2N\text{–}C_6H_4\text{–}NMe_2)^{+}$$

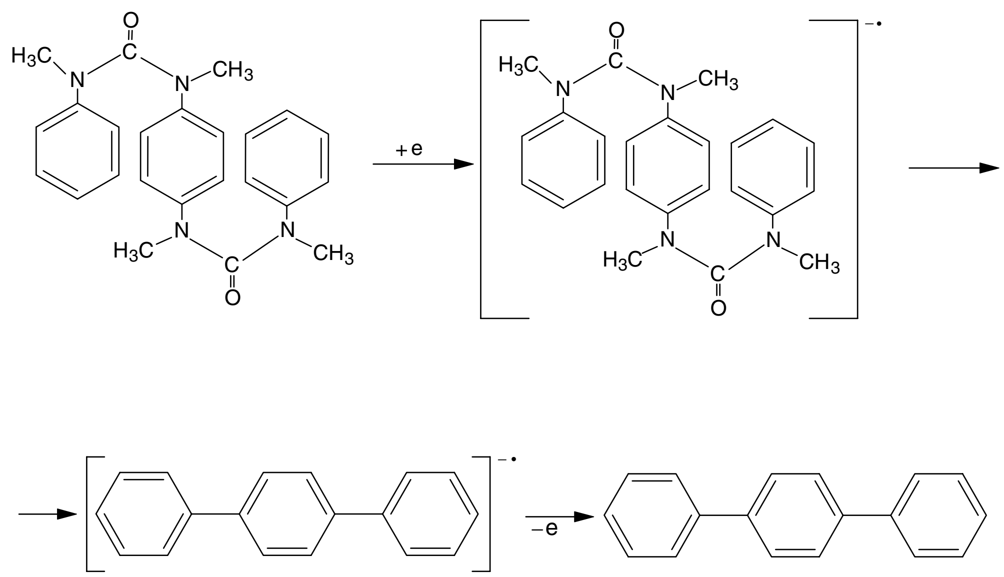
The decomposition of organic nitroso compounds with the generation of nitrogen oxide attracts the attention of biochemists as well. Initiating many important reactions in living organisms, nitrogen oxide acts as a *biochemical synthon*. Note that the C–N bond breaking is easier for *t*-$BuNO^{+\bullet}$ than for neutral *t*-BuNO by approxiamtely 165 kJ·mol^{-1} (Greer et al. 1995). This suggests extreme weakness of the C–N bond in nitroso cation-radicals. Therefore, the behavior of 1-nitrosoadamantane (1-Ad-NO) on one-electron oxidation is interesting. The C–N bond of 1-Ad-NO is no doubt stronger than that of *t*-BuNO. Chemical oxidation of this nitrosocompound by tris(2,4-dibromophenyl)ammoniumyl hexachloroantimonate in AN results in denitrosation. On aqueous workup, 1-adamantylacetamide is formed. Greer et al. (1995) proposed the following sequence for this oxidative C–N bond cleavage:

$$\text{1-Ad-NO} - e \rightarrow (\text{1-AdNO})^{+\bullet} \rightarrow NO^{\bullet} + [\text{1-Ad}^{+}]$$

$$[\text{1-Ad}^{+}] + \text{MeCN} \rightarrow [\text{1-Ad-N}^{+}\equiv\text{C–Me}]$$

$$[\text{1-Ad-N}^{+}\equiv\text{C–Me}] \rightarrow \text{1-Ad-NHCOMe}$$

Anion-radicals of the *N*-methylated arylurea oligomers undergo an intramolecular elimination of the *N*-methyl carbamide moiety. They come out as synthons for linear polyarylenes (Kurth et al. 2003, Lewis et al. 2004). Note that polyphenyls have attracted great interest as elements of supramolecular assembled devices, semiconductors, and light-emitting diodes. Linear terphenyl is used as a high-temperature heat carrier. Its manufacturing consists of passing of benzene vapors over



SCHEME 7.58

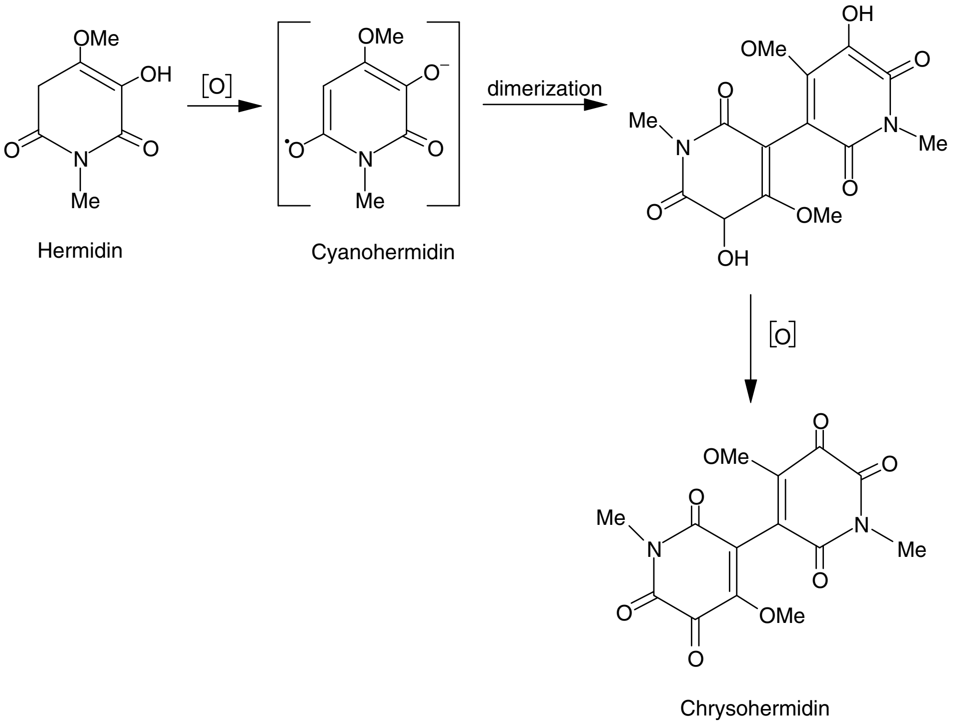
copper or cobalt deposited on ceramics. The anion-radical method consists simply in the contact of an oligomer with alkali metal in HMPA. Scheme 7.58 shows the sequence of the transformations leading to the formation of terphenyl anion-radical. The reaction is applicable to many-layered phenyl methyl ureas and the analogs containing biphenyl, naphthyl, and anthryl fragments. The final anion-radicals can be readily oxidized to the neutrals, whereas the starting arylureas can be easily prepared from arylamine and diamine building blocks. Lewis et al. (2004) suggests that urea linkers split off as *N,N′*-dimethyldiaziridinone. The latter then transforms into some polymeric material. In the initial (neutral) substances, aryl rings are drawn together so that the distance between the ring carbon atoms attached to the urea linkers is not more than 0.3 nm. This distance is smaller than the sum of van der Waals radii. The π,π interaction between the rings is weak, but it becomes more pronounced after one-electron reduction (Baumgarten et al. 2000). Such a tightening is supposedly achieved by the jumping of an unpaired electron between these adjacent rings. Binding the rings preserves their sequencing.

7.7 BOND FORMATION

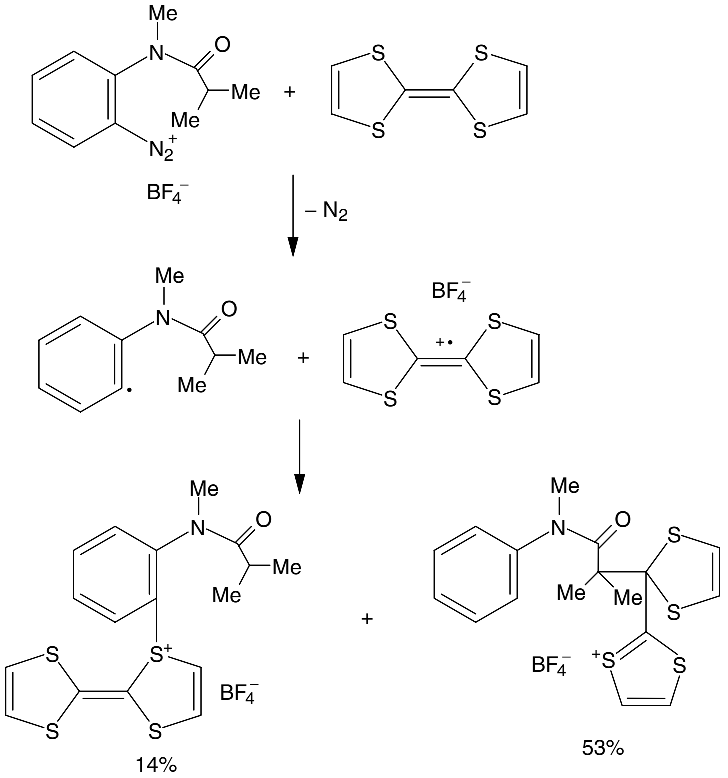
Nucleophilic and electrophilic substitutions in anion- and cation-radical, respectively, have been considered throughout the book, including the problem of a choice between addition and electron-transfer reactions. Therefore, only some unusual cases are discussed here.

An interesting process of C–C bond formation is represented by the autooxidation of *Mercurialis perennis* L. plant alkaloid hermidin. The reaction proceeds through the formation of a transient blue anion-radical, which dimerizes with the transfer of the reaction center to give, eventually, chrysohermidin as a dimeric hexaketone (Wasserman et al. 1993; Scheme 7.59).

The redox reaction shown in Scheme 7.60 results in the formation of an amide σ-radical and tetrathiafulvalene cation-radical. These initially formed σ-radical and cation-radical combine to give salts of the S-arylated tetrathiafulvalene (a minor product) and C-alkylated tetrathiafulvalene (the main product). The latter demonstrates an unprecedented carbon–carbon bond formation with the cation-radical of tetrathiafulvalene; the structure depicted was confirmed by single crystal x-ray analysis (Begley et al. 1994).



SCHEME 7.59



SCHEME 7.60

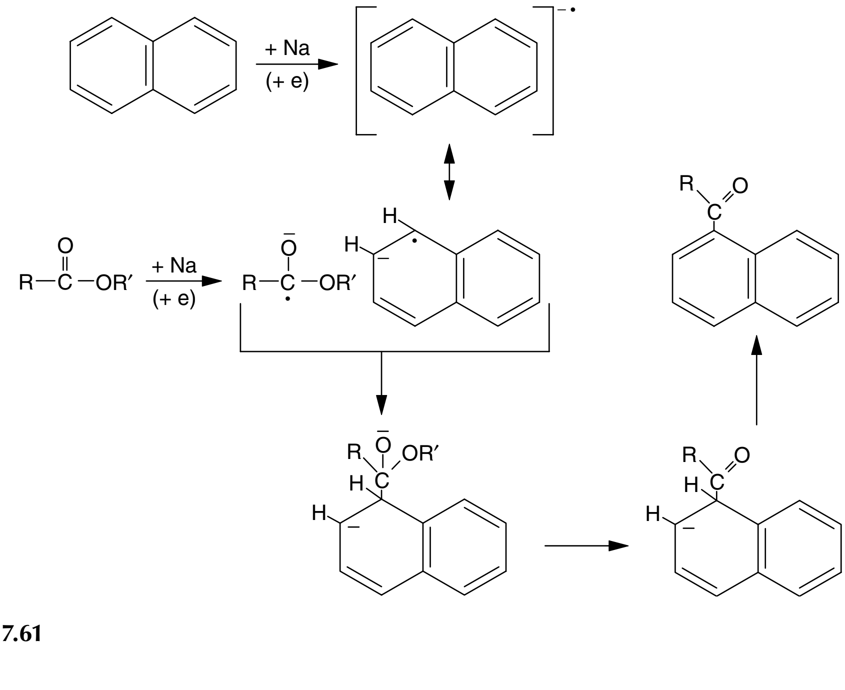
As for the σ-radical participant in this coupling reaction, the main product is surely formed as a result of radical translocation. As for the cation-radical participant, the position of the coupling is explained as follows (Begley et al. 1994):

> Calculations indicate that the unpaired electron density in the cation-radical of tetrathiafulvalene resides principally on sulfur, but with the internal carbon being the site of second highest density. The product of coupling of an α-carbonyl radical to sulfur, an α-carbonyl–sulfonium salt would be destabilized by the adjacent dipoles. The transition state would be expected to mirror this, thus slowing down the C–S coupling and permitting the observed coupling to the carbon of tetrathiafulvalene.

This is not only unprecedented, but also a promising feature in terms of organic metal preparation (see Chapter 8). The C–C bond formation consists of coupling the radical with the cation-radical.

Nemykin et al. (2007) found a similar direct reaction between ferrocene (FcH) and tetracyanoethylene (TCNE). The formation of a spectroscopically detected {$[FcH]^{+\bullet}$ $\bullet[TCNE]^{-\bullet}$} was established. Cyanoferrocene and tricyanovinylferrocene as major and minor products were obtained, respectively. Although tricyanovinylferrocene was not the sole product of this reaction and its yield was approximately 30%, the direct method of its preparation was an important step toward materials for optically limiting devices. Untill now, the highly toxic chloromercurioferrocene was used for the preparation of tricyanovinylferrocene (Nemykin and Kobayashi 2001).

The coupling between two different anion-radicals can also lead to the C–C bond formation; Section 3.2.1 mentions one such example. Another example, more relevant from the synthetic point of view, is as follows. Anion-radicals, prepared by the addition of alkali metals to aromatic hydrocarbons in THF, react with aliphatic esters to give the corresponding acylated products with good yields (Periasamy et al. 1999). Thus, the reactions of sodium naphthalene, sodium anthracene, or sodium phenathrene with ethyl formate yield the corresponding aldehydes. Sodium naphthalene gives *n*-propyl-1-naphthyl ketone or methyl-1-naphthyl ketone on reaction with methyl butanoate or ethyl acetate, respectively. All the aromatic anion-radicals yield the corresponding aldehydes on treatment with *N*,*N*-dialkylformamides. The authors rationalized the results through the mechanistic pathway as shown in Scheme 7.61. As the authors mentioned, use of more than two equivalents



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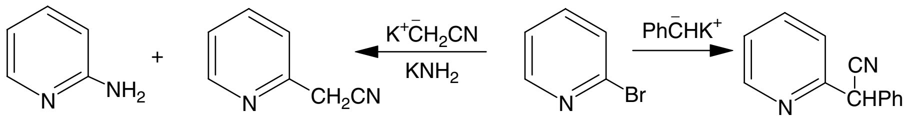


SCHEME 7.62

of sodium is necessary to obtain the products in reasonable yields—one equivalent is needed for the formation of an aromatic anion-radical and another is used up for the formation of an anion-radical derived from ester.

Generally, several other methods of formylation and acylation exist in the organic synthesis repertoire. Nevertheless, the procedure described here is useful, for it uses inexpensive starting materials.

Nucleophilic reactions between various carbanions (nucleophiles) and heteroaromatic compounds are used in the syntheses of physiologically active compounds (Wong et al. 1997). Let us consider the photoassisted reaction between 2-bromopyridine and carbanions, which are stabilized by cyano group, as an example. The potassium derivatives of AN and phenylactonitrile were compared (Moon et al. 1983). To obtain the corresponding carbanion, a nitrile is treated with potassium amide in liquid ammonia. Phenylacetonitrile is a stronger CH acid than AN. Phenylacetonitrile forms the potassium derivative quantitatively, whereas AN reacts with potassium amide reversibly. Interacting with 2-bromopyridine, phenylacetonitrile-potassium gives solely pyridyl phenyl acetonitrile, whereas acetonitrile-potassium produces a 3:1 mixture of pyridyl acetonitrile with aminopyridine (Scheme 7.62).

If di(*tert*-butyl)nitroxide (a radical trap) is present, the reaction with phenylacetonitrile-potassium does not proceed entirely. Acetonitrile-potassium (which is in equilibrium with potassium amide) forms only aminopyridine in the presence of the trap (Moon et al. 1983). Consequently, amination is a classical nucleophile reaction, and the formation of pyridyl acetonitrile is a reaction of the $S_{RN}1$ type. These two reactions are quite different. A stronger CH acid leads to a well-defined synthesis.

The results obtained in the photostimulated $S_{RN}1$ reaction between carbanions from 2,4,4-trimethyl-2-oxazoline or 2,4-dimethylthiazole and 2-bromopyridine are also consistent with the incomplete formation of the carbanions in KNH_2–$NH_{3(liq)}$ system. In these cases, 2-aminopyridine is formed alongside the corresponding pyridyl-2-methylene oxazolinyl or thiazolyl substitution products (Wong et al. 1997). When the $S_{RN}1$ pathway is impeded by conducting the reaction in the dark or in the presence of di(*tert*-butyl) nitroxide, the ionic amination reaction dominates.

The synthesis of pyridines containing an arylated methylene group belongs to the same $S_{RN}1$ type of substitution reactions. These derivatives serve as starting materials in the manufacturing of various medications. Methylpyridines can easily be transformed into methylencarbanions on metallation. The carbanions were commonly used in reactions with compounds bearing strong departing groups such as bromide or trialkyl ammonium. These reactions were recognized as typically nucleophilic ones. To promote them, usual methods were employed (e.g., increase in temperature or pressure). The synthesis of dipyridyl methane based on 4-chloropyridine and sodium derivative of 4-methylpyridine can serve as an example (Wiberg and Lewis 1970, Gaus et al. 1977). The yields were usually not high and nonreproducible. The yield turned out well when ion-radical mechanism of the transformation was revealed. An inert atmosphere is needed for the reaction; the transformation should be stimulated by photoirradiation instead of condition toughening such as an increase in temperature or pressure. This provided stable and high yields (Moon et al. 1983, Bunnett and Glooz 1974). Section 7.8 gives a concise review of oppurtunities associated with $S_{RN}1$ reactions.

The electrochemical behavior of 1-fluoro-2,4-dinitrobenzene, 1-chloro-2,4-dinitrobenzene, and 1-bromo-2,4-dinitrobenzene in DMF was described (Gallardo et al. 2000) as follows. The 1-fluoro-2,4-dinitrobenzene anion-radical dimerizes *before* cleavage, whereas 1-chloro-2,4-dinitrobenzene

and 1-bromo-2,4-dinitrobenzene anion-radicals dimerize *after* cleavage. The preliminary cleavage led to the formation of 2,4-dinitrobenzene from the chloro- and bromoderivatives. In the case of the fluoroderivative, the change in mechanism allowed to obtain 2,2′,4,4′-tetranitrobiphenyl selectively and with good efficiency. In a synthetic context, the dimerization of anion-radicals before carbon–halogen bond breaking in these substrates can be very significant since the Ullmann method, the classical synthesis of biphenyls, has not been described for 2,2′,4,4′-tetranitrobiphenyl. The latter is obtained alternatively by nitration of biphenyl (Conforth 1996). The ion-radical route opens a new, convenient and safe, method to synthesize this nitro compound, which is important in polymer chemistry. The energy of carbon–halogen bond dissociation is the dominant factor responsible for the difference uncovered (Gallardo et al. 2000).

7.8 OPPORTUNITIES ASSOCIATED WITH $S_{RN}1$ REACTIONS

This type of organic reaction is important and deserves some comments. The addition of one electron to a molecule generates an anion-radical. This results in an increase in its reactivity. Particularly, the bond dissociation energies in anion-radicals are much smaller than those in the corresponding neutral molecules. Thus, substitution reactions proceed more easily in the case of anion-radicals. The reactions of the $S_{RN}1$ type are good examples of this feature. Two possible schemes (a and b) for the reaction course are listed as follows:

Scheme a

$$(RX)^{-\bullet} \rightarrow X^- + R^\bullet;\ R^\bullet + Nu^- \rightarrow (RNu)^{-\bullet};\ (RNu)^{-\bullet} + RX \rightarrow RNu + (RX)^{-\bullet}, \text{ etc.}$$

Scheme b

$$(RX)^{-\bullet} \rightarrow X^- + R^\bullet;\ R^\bullet + Nu^- \rightarrow (RNu)^{-\bullet};\ (RNu)^{-\bullet} + RX \rightarrow RNu + X^- + R^\bullet, \text{ etc.}$$

Substitution of scheme a forms a well-documented class of reactions (see Costentin et al. 1999, 2000, Costentin and Saveant 2000, Corsico and Rossi 2000, 2002, 2004, Adcock et al. 2001, Vanelle and Crozet 2002, Medebielle et al. 2002, Galli and Rappoport 2003, Rossi et al. 2003, Vanelle et al. 2004, and Buden et al. 2005 and references therein). In contrast to conventional nucleophilic substitution, the nucleophile, Nu^-, reacts not with the substrate, RX, to give a product but with the radical $R^\bullet$. The latter emerges as a result of R–X bond cleavage. Substituent X is very often a halogen atom, but other leaving groups can also be used (see section 7.8.1). In the majority of aromatic $S_{RN}1$ reactions, the anion-radical $RX^{-\bullet}$ (R=Ar) is the observable intermediate. It is depicted in scheme a. With aliphatic substrates, $S_{RN}1$ substitution takes place rather than S_N2 or S_N1 substitutions, and the concerted mechanism depicted in scheme b is feasible.

In most cases, the coupling reaction between the radical and nucleophile species is the rate-determining step in the dark (see, e.g., Tamura et al. 1991, Azuma et al. 1992). This step leads to the formation of $RNu^{-\bullet}$, the product of real substitution. The chain process is completed by a reaction in which one electron is transferred from the product anion-radical to the substrate. A neutral substitution product is formed; the propagation loop is closed.

It is logical to consider the nucleophile, Nu^-, as a source of the electron to be transferred onto the substrate molecule, RX. However, in most cases, the nucleophile is such a poor electron donor that electron transfer from Nu^- to RX is extremely slow, if it is possible at all. These reactions require an external stimulation in which a catalytic amount of electrons is injected. Such kinds of assistance to the reactions from photochemical and electrochemical initiations or from solvated electrons in the reaction mediums have been pointed out earlier. Alkali metals in liquid ammonia and sodium amalgam in organic solvents can serve as the solvated electron sources. Light initiation is also used widely. However, photochemical initiation complicates the reaction performance.

A concise description of the requirements concerning the substrate structure, nature of the introducing group, and reaction medium is discussed in the following text.

7.8.1 Substrate Structure

The groups to be substituted as a result of the $S_{RN}1$ reaction must be stable in the form of the corresponding ion. Other substituents (not participants in the transformation) must be inert electrochemically, that is, they must be insensitive to electron transfer.

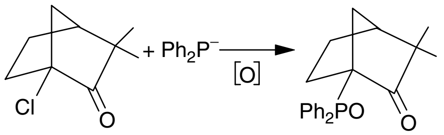
Halogens are substituents of good fugacities. Iodine and bromine demonstrate practically equal activity during photostimulated substitution. Therefore, the more accessible derivatives can be used. Groups such as SPh, Me_3N^+, $OP(O)(OEt)_2$ are also substituted readily, especially in aromatic substrates. Alkyl and alkoxy groups do not prevent the substitution. Steric shielding of alkyl groups is insignificant. For instance, the reaction rates of *o*- and *p*-halotoluenes are practically equal. The $S_{RN}1$ reaction does not take place in case of hydroxy or dialkylamino derivatives of halobenzenes (Wolfe and Carver 1978). There are many excellent examples of easy preparation of hindered compounds with significantly screened centers.

The reaction is assisted by π acceptors (carbonyl, phenyl) through an intramolecular electron transfer to the leaving group. This intramolecular redox catalysis is well illustrated by comparing 1-chloronorbornane and its 2-carbonyl analog. The former is nonreacting toward Ph_2P^- under photoirradiation; the latter does react to give, after oxidation, the substitution product in 93% yield (Rossi et al. 2003; Scheme 7.63).

The ketone receives an electron in the antibonding π^* MO to form π^* anion-radical, which is transformed into a $(\text{–C–Cl})^{-\bullet}$ moiety by an intramolecular electron transfer to the antibonding σ^* fragmental orbital of the –C–Cl bond. The $(\text{–C–Cl})^{-\bullet}$ moiety then fragments to form a chloride ion and the corresponding radical (Scheme 7.64).

The photostimulated reaction of 4-chlorocamphor (in which the spatial distance between the leaving chloride and the C=O function is increased with an extra C–C bond) yields, after oxidation, an organophosphoric product in 80% yield (Rossi et al. 2003; Scheme 7.65).

Unlike conventional nucleophilic substitution, the cyclopropane ring does not cleave during $S_{RN}1$ reactions of Schemes 7.64 and 7.65. Another common feature of these two reactions consists



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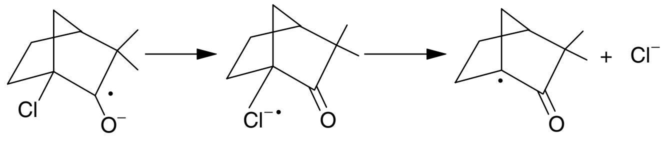

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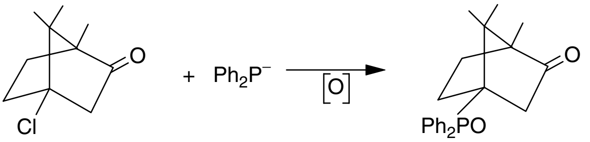

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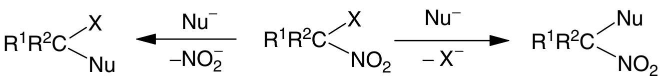


SCHEME 7.66

of the carbonyl group effect. Being a π substituent, the carbonyl group accepts an entering electron, passes it to the chlorine-containing position and thereby assists in the chloride elimination. The authors name this phenomenon as *intramolecular* π *catalysis* (Rossi et al. 2003, Uranga et al. 2006). Importantly, the reactions depicted for the norbornane and camphor derivatives consist of photostimulation as the indispensable condition of the whole substitution.

The influence of the nitro group depends on the general nature of the substrate. The presence of a nitro group is sometimes unfavorable. However, the substitution at a saturated carbon atom is strongly facilitated if the nitro group is bonded with the same carbon atom that bears a leaving group. In this case, either X or NO_2 can come off (Scheme 7.66).

The nature of X governs the splitting preference. If X = I, Br, Cl, $S(O)_2R$, S(O)R, SR, or SCN, the leaving group is just X. NO_2 is eliminated when X = C(O)R, C(O)OR, RPO_3, NO_2, CN, N_3, or Alk (Bowman 1988, Al-Khalil et al. 2001). In the substrates of Scheme 7.66, both X and NO_2 are located at the same tetrahedral carbon atom. The first step of the reaction consists of the formation of the substrate anion-radical. The unpaired electron apparently occupies the orbital centered on the nitrogen atom of the nitro group. Substituent X is in the zone of influence of this orbital. Being in this zone, substituent X can recapture the unpaired electron of this orbital. Favorable factors are the C–X bond lability and X^- fugacity. In contrast, if X^- fugacity is small and C–X bonding is strong, then NO_2^- turns out to be the leaving group.

A cation arriving with a nucleophilic anion is another important factor. The nucleophile can attack the substrate in the form of a free ion or an ionic pair. As a rule, lithium salts are less reactive than sodium and potassium salts. Russell and Mudryk (1982) reported several examples of this. The sodium salt of ethyl acetylacetate reacts with 2-nitro-2-chloropropane in DMF yielding ethyl 2-(*iso*-propylidene) acetylacetate. Under the same conditions, the lithium salt does not react at all. Potassium diethyl phosphite interacts with 1-methyl-1-nitro-1-(4-toluylsulfonyl)propane in THF and gives diethyl 1-methyl-1-nitro-1-phosphite. The lithium salt of the same reactant does not react with the same substrate in the same solvent.

Transformation of a substrate into its ion-radical enhances the reactivity of the species. Sometimes, this can overcome steric encumbrance of the substituent to be removed. Thus, in the case of 1,4-diiodo-2,6-dimethylbenzene the photoinitiated action of the enolate ion of pinacolone ($Me_3CCOCH_2^-$), led to substitution of both iodines (from positions 1 *and* 4) (Branchi et al. 2000).

7.8.2 Nature of Introducing Groups

There are two important requirements for reagents in $S_{RN}1$ reactions. They have to be electron donors with respect to the substrates or active interceptors of intermediary radicals. For example, the phenyl thiolate and diphenylphosphite ions are active in such interception; the phenolate ion is inactive. The introducing group sometimes exerts an influence on chain branching. All of these peculiarities are detailed in Chapters 3 through 5.

7.8.3 Reaction Medium

The reactions under consideration often require an inert atmosphere. However, some examples can be found in Chapters 4 and 5 when air and even pure oxygen atmospheres are optimal.

As for solvents, liquid ammonia or dimethylsulfoxide are most often used. There are some cases when *tert*-butanol is used as a solvent. In principle, ion-radical reactions need aprotic solvents of expressed polarity. This facilitates the formation of such polar forms as ion-radicals are. Meanwhile, the polarity of the solvent assists ion-pair dissociation. This enhances reactivity of organic ions and sometimes enhances it to an unnecessary degree. Certainly, a decrease in the permissible limit of the solvent's polarity widens the possibilities for ion-radical synthesis. Interphase catalysis is a useful method to circumvent the solvent restriction. Thus, 18-crown-6-ether assists anion-radical formation in the reaction between benzoquinone and potassium triethylgermyl in benzene (Bravo-Zhivotovskii et al. 1980). In the presence of tri(dodecyl)methylammonium chloride, fluorenylpinacoline forms the anion-radical on the action of calcium hydroxide octahydrate in benzene. The cation of the onium salts stabilizes the anion-radical (Cazianis and Screttas 1983). Surprisingly, the fluorenylpinacoline anion-radicals are stable even in the presence of water.

Similarly, interphase catalysis permits carbonylation of haloaryls and halovinyls by $NaCo(CO)_4$ with CO in water. The reaction proceeds according to $S_{RN}1$ mechanism and leads to high enough yields of carboxylic acids. Because C_{Ar}–Cl bond is inert in these conditions, the direct and selective synthesis of chlorocarboxylic acids becomes possible. Thus, 1-bromo-4-chlorobenzene gives 4-chlorobenzoic acid only (Brunet et al. 1983; Scheme 7.67).

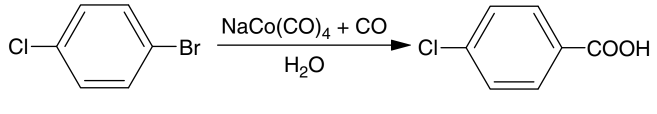
During initiation with metal ions, a solvent can play the role of a donor ligand to this metal ion and thus enforce its activity. An example from SmI_2 chemistry is as follows: In mixtures of HMPA and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)pyrimidinone with AN (but not with THF), the rate of reductive cyclization of *o*-allyloxyiodobenzene with SmI_2 sharply increases (Hasegawa and Curran 1993).

7.8.4 Dark $S_{RN}1$ Reactions

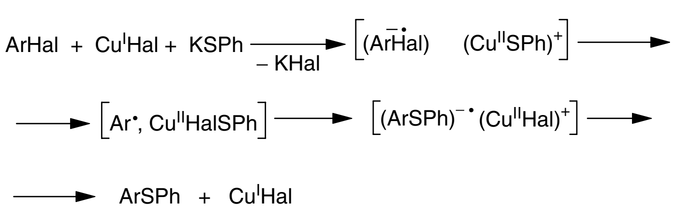
Photostimulation increases the number of reagents and substrates that can be involved with $S_{RN}1$ reactions. However, it complicates their performance (see review by Ivanov 2001). Therefore, the dark reactions are of special interest.

The photoirradiation effect can be replaced by copper salt catalysis. The catalyzed reactions proceed rapidly and result in a high degree of transformation. Interestingly, ESR method reveals no organic paramagnetic particles in the course of the reaction between haloaryls and phenyl thiolates. The addition of oxidants (oxygen and DNB) or radical acceptors (di(*tert*-butyl)nitroxide) does not inhibit the substitution. These facts are understandable from Scheme 7.68 (Bowman et al. 1984, Liedholm 1984).

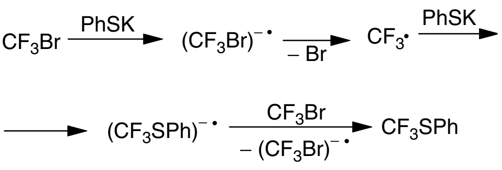
Several substitution reactions are catalyzed by iron ions (Galli and Bunnett 1984). A detailed preparative study was reported on the ferrous ion-initiated $S_{RN}1$ reactions of haloarenes with the



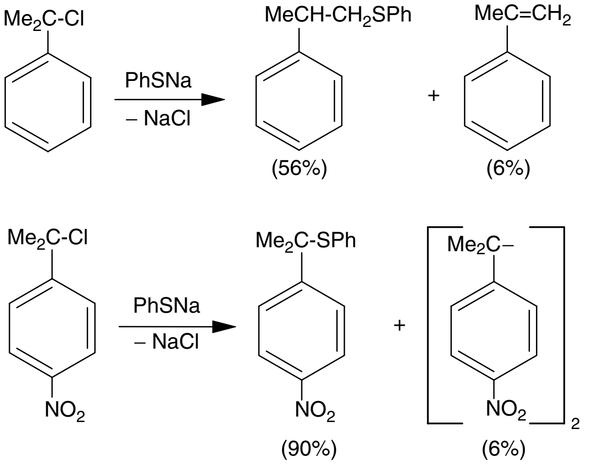
SCHEME 7.67



SCHEME 7.68



SCHEME 7.69



SCHEME 7.70

sodium enolates of *tert*-butyl acetate, *N*-acetylmorpholine, and a number of higher *N*-acylmorpholines. Smooth and rapid substitution occurs and good to excellent yields were obtained for arylacetic esters, arylacetamides, and arylalkyl amides. The catalytic activities of cuprous chloride, ruthenium trichloride, mercuric sulfate, cobalt sulfate, and dicerium trisulfate were also mentioned (van Leeuven and McKillop 1993).

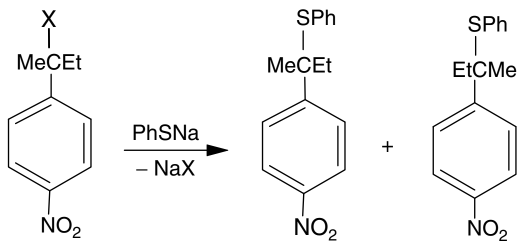
Some $S_{RN}1$ reactions can take place in the dark without a catalyst. For example, the interaction of freons with nucleophiles in DMF at 20°C proceeds without photoirradiation. The chain process begins when the system pressure reaches 2 atm, in other words, when the concentration of the gaseous reagent becomes sufficient (Wakselman and Tordeux 1984; Scheme 7.69). There is a favorable difference between the ionization potential of the nucleophile (PhS^-) and EA of the substrate (CF_3Br); the expressed bromide fugacity is also a favorable factor.

The Kornblum reactions at the tertiary carbon atoms also proceed as the dark $S_{RN}1$ substitutions. Let us compare the reactions of α-cumyl chloride and 4-nitro-α-cumyl chloride with phenylthiolate ion (Kornblum 1975; Scheme 7.70).

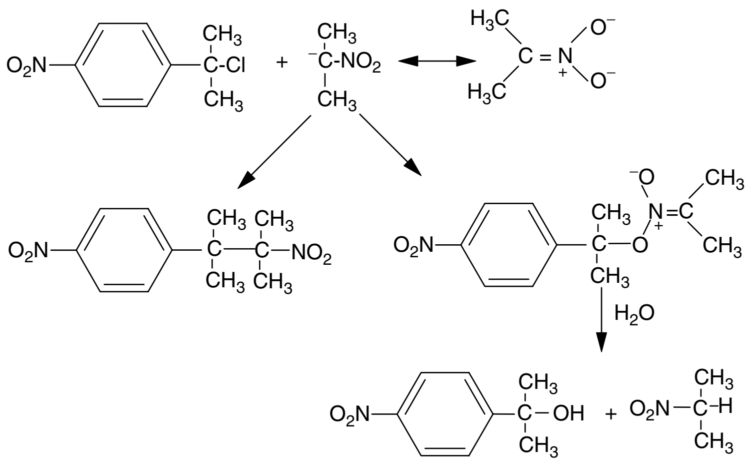
As seen, the direct substitution of the arylthio moiety for chlorine is observed only for the 4-nitro derivatives. The optically active substrate gives the racemic substitution product on the reaction with phenylthiolate ion (Scheme 7.71).

Radical inhibitors and electron acceptors prevent the formation of the substituted product. Oxygen drastically retards the substitution but facilitates the formation of *p*-nitrocumyl peroxide. Photoirradiation somewhat accelerates the reaction. Consequently, the reaction is of the ion-radical type. The nucleophile (PhS^-) is sufficiently active as an electron donor and a radical interceptor. The reaction does not need photostimulation.

The reaction of the same 4-nitro-α-cumyl chloride under the same conditions but with another nucleophile, the 2-nitropropanide ion, leads principally to the same result. This reaction was studied



SCHEME 7.71



SCHEME 7.72

by Costentin and Saveant (2000). The only species that might provide stimulating electrons to the system is the nucleophile (the nitropropenide ion). However, this nucleophile is such a poor donor that electron transfer from this ion to 4-nitro-α-cumyl chloride is expected to be extremely slow, apparently too slow to serve as a viable initiation step. Costentin and Saveant tried to solve such an enigma. Their strategy was to identify the reaction product, measure the reaction kinetics, and determine all of the thermodynamic and kinetic factors of initiation, propagation, and termination. The authors wondered what the reaction kinetics should be if the nucleophile was the electron donor initiator, and they compared the results with the experimentally obtained data. They carried out this reaction under pseudo-first-order conditions (excess of 2-nitropropanate ions) in AN at 25°C, under an argon atmosphere in a light-protecting vessel. The 2-nitropropanate ion was introduced as tetramethylammonium salt. Two products were formed (see Scheme 7.72).

One of the products was the expected C-substituted compound. The other was an unstable species, which decomposed into 4-nitrocumyl alcohol during workup and was ascribed to O-substitution. Kornblum (1975) had obtained the same products. He considered the C- and O-substitution as $S_{RN}1$ and S_N2 reactions, respectively. Dual reactivity of nucleophiles is well known. Since steric hindrance at the reacting carbon prevents S_N2 reaction with 4-nitrocumyl chloride, Costentin et al. (1999) concluded that both the C- and O-substitution products result from an $S_{RN}1$ reaction.

The $S_{RN}1$ character of the reaction was ascertained by the effect of light irradiation and addition of a radical trap. Namely, under light irradiation, the half-reaction time was considerably shortened (3 instead of 41 min). Addition of di(*tert*-butyl)nitroxide completely quenched the reaction—neither C- nor O-substitution was observed after 4 h. The radical trap may only react with the $R^\bullet$ radicals that escaped the solvent cage where $R^\bullet$, $Nu^\bullet$, and X^- have been formed. This means that, in the

absence of the trap, the R• radical does react with Nu• before diffusing out of the cage. The fact that the radical trap quenches the formation of both the C- and O-substitution products confirms that both species result from an $S_{RN}1$ reaction.

The outer-sphere electron-transfer initiation mechanism cannot account for the observed kinetics, the half-reaction time being more than 100 times greater than that observed. The chain process considerably enhances the global rate of the reaction (without a chain process, the half-reaction time would be three centuries).

The solution of the riddle posed by Kornblum's dark $S_{RN}1$ reaction is as follows. The nucleophile does work as a single electron-transfer initiator of the chain process. However, the mechanism of initiation does not consist of a mere outer-sphere electron transfer from the nucleophile to form the anion-radical of the substrate. Rather, it involves a dissociative process in which electron transfer and bond breaking are concerted (Costentin and Saveant 2000). Scheme b at the beginning of Section 7.8 illustrates the concerted mechanism.

The passage from a stepwise (the phenylthiolate ion as a nucleophile) to a concerted mechanism (the nitropropanate ion as a nucleophile) is a consequence of the low driving force offered by the poor electron-donor properties of the nucleophile.

7.9 CONCLUSION

Within our previously stated restrictions, this chapter has considered some selected syntheses. Possible generalizations were made as well. This chapter should be correlated with the data from other chapters of the book. Usage of mild reagents, reaction conditions, and new methodologies promise forthcoming breakthroughs in the area of ion-radical synthesis. Their utility in synthetic strategies has only now begun to be exploited.

Organic chemistry has many diversified synthetic methods; the ion-radical methods are among them. This chapter shows the features and specific advantages of ion-radical approaches to needed compounds, having no intention to strike out other synthetic routes.

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8 Ion-Radical Organic Chemistry in Its Practical Applicability

8.1 INTRODUCTION

The aim of this part of the book is to look at current practical applications of organic ion-radical chemistry. Chapter 8 examines patents and original (experimental) papers that offer commercial advantages compared with conventional approaches. It pays special attention to newly developed branches of material science that may become technically important in the near future. Ion-radical organic chemistry opens new possibilities in the synthesis of material for molecular electronic applications, including problems connecting with microelectronic core materials, organic metals, and magnets. A special section of the chapter is devoted to study the mechanism of lubrication during the rubbing of metallic surfaces. The other one considers ion-radical reactions taking place in industrial cooking of woods and fuel desulfurization. It is difficult to overestimate technical importance of all these problems.

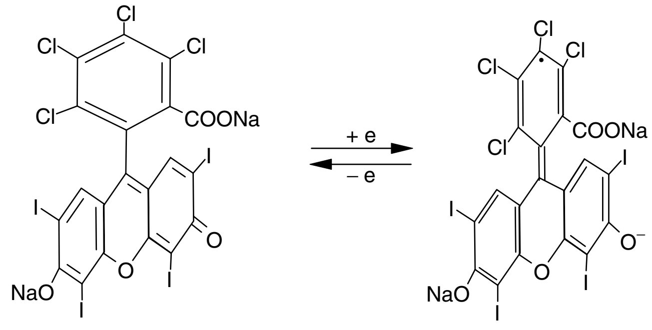
8.2 ORGANIC ION-RADICALS IN MICROELECTRONICS

The creation of new systems to record, store, and reorganize information is one of the main tasks in the development of microelectronics. At present, there are working systems that organize information from optical or electrical signals (Fisher et al. 1976). However, it is reasonable to use one of these signals for recording and another for organizing the information accepted. This avoids the use of complicated electronic and optical switches and allows the use of two separate sources of signals, electronic and optical. As a result, the device is simplified significantly. Another important problem is in switching to a high-conducting state by electrode reduction of organics. Ion-radical organic chemistry can propose such basic materials satisfying microelectronic strategy, as exemplified by the following sections.

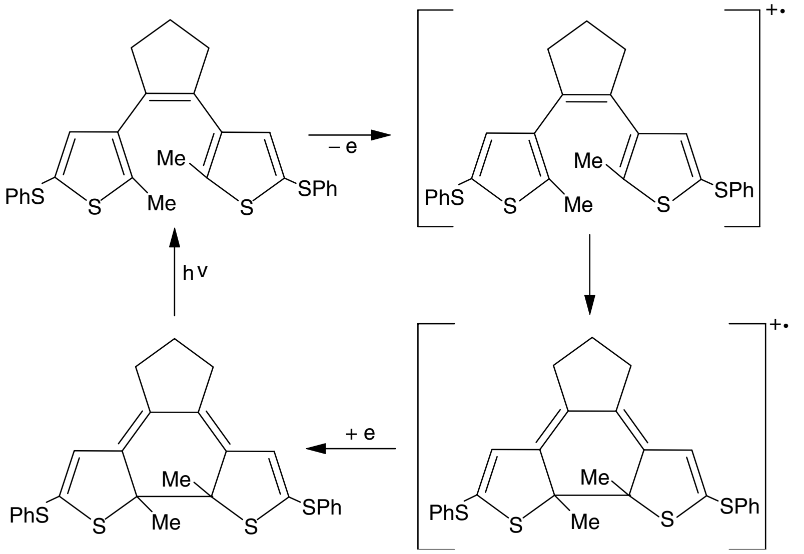
8.2.1 ION-RADICAL APPROACH TO MOLECULAR SWITCHES AND MODULATORS

To switch between low- and high-conducting states, Bandyopadhyay and Pal (2004) proposed a device that contains indium tin oxide on a glass support. The film containing polyallylamine hydrochloride (the solid polyelectrolyte) and Rose Bengal (the core organic material) is placed above the oxide. On the top of the film, evaporated aluminum is situated. This is the complete electrode system. At weak voltage, electric conductivity of the system is low. A definite increase in the voltage enhances the conductivity markedly. Chemically, Rose Bengal in its neutral state (and when the voltage is low) exists in the conformation where xanthenyl and phenylcarboxylate fragments are perpendicular to each other. The higher voltage gives rise to the semiquinone anion-radical in which both the planes become coplanar and conjugation system spreads over the whole molecular framework. Moreover, the presence of an unpaired electron enhances dipole moment and the fully conjugated anion-radical orients toward the direction of the electric field. Scheme 8.1 represents this principle to perform a "write-read-erase-read" sequence.

Accumulation and reorganization of information can also be achieved on the basis of cis–trans isomerization of olefins in their ion-radical states. An application of the phenomenon in real electron memory systems was claimed (Todres 2001). For the neutral arylethylenes, conversion from



SCHEME 8.1



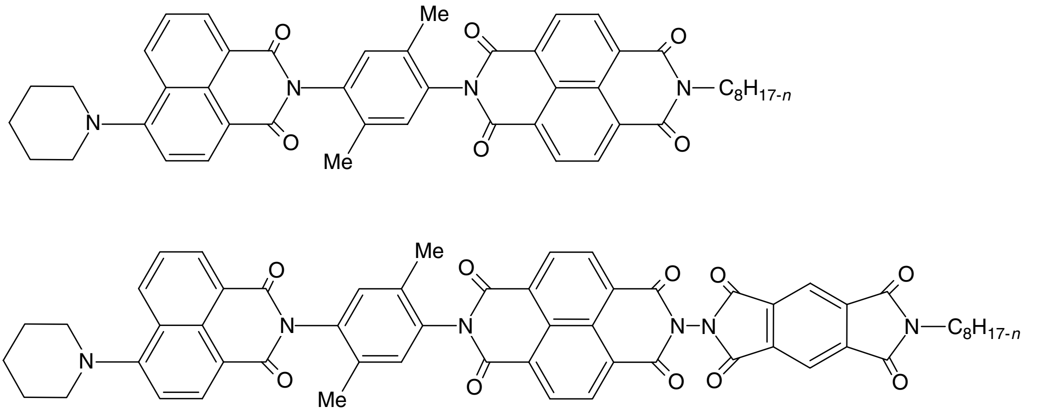
SCHEME 8.2

cis to trans results in a bathochromic shift of their absorption bands of 20–25 nm and in a 100- to 250-fold increase in absorption; the reverse trans-to-cis transformation can occur only upon light irradiation. Therefore, the materials based on these photochromic compounds exhibit enhanced sensitivity to light. They also acquire sensitivity to electric impulse and ability to keep the information recorded.

If *cis*-arylethylenes are used as electrochromic substances (in media capable of conducting electric current), applying a 10- to 12-V cyclically changing voltage enhances the optical absorption as described earlier. These changes are readily registered and remain constant for at least 2 years. In order to return to the initial state of the system, it is sufficient to apply a near-UV light impulse for just a few seconds. The record-erase cycles can be repeated more than 1000 times with the same capacity.

Exploiting arylethylenes as bearers of electron memory has the following advantages: First, the compounds are commercially available and inexpensive. Second, they work for very long time. Third, transformation of the information recorded is simple and consumes little energy. In other words, creation of electron memory systems through ion-radical route is fruitful.

The dithienylcyclopentene family also presents electrochromism with memory (Peters and Branda 2003; Gorodetsky et al. 2004; Zhou et al. 2004; Guirado et al. 2005). Scheme 8.2 gives a



SCHEME 8.3

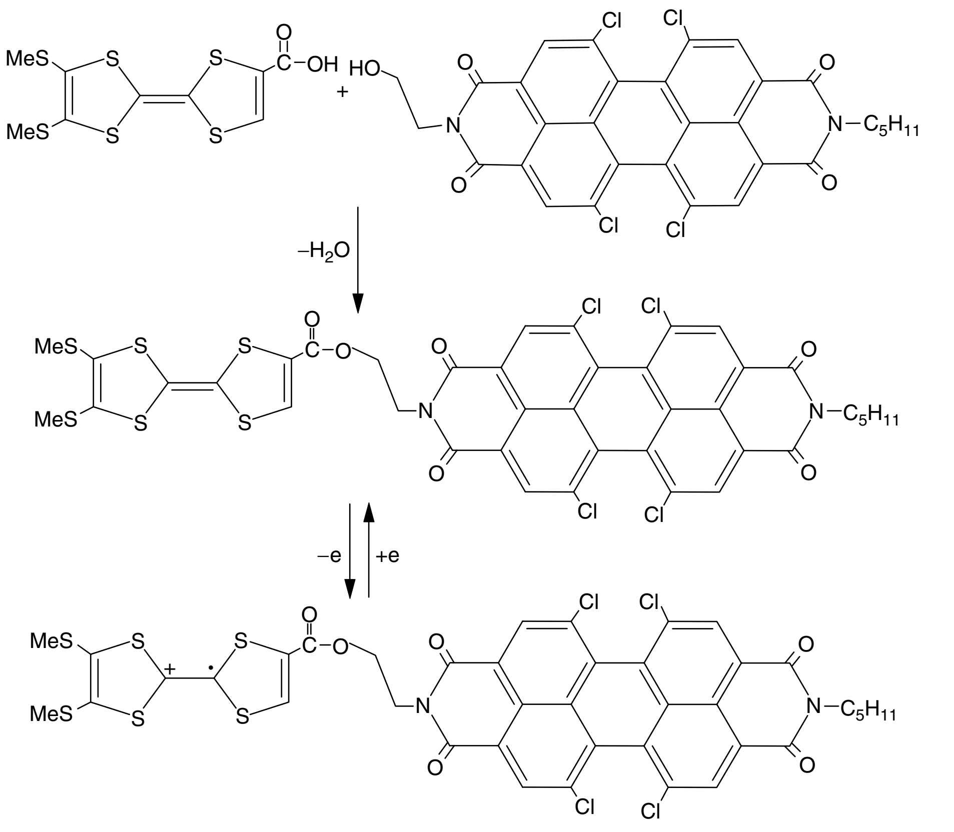
sketch of such a redox process initiated by the formation of a dithienylcyclopentene cation-radical. In the sketch, the open structure is colorless, and the closed one is tinted. The ring-closed isomer is transformed to the opened one by light irradiation. Coloration and bleaching that result from the combination of the redox and photoreactions, form the basis of devices named dual-mode chemical signal transducers with distinctive color changes (Zhi et al. 1995).

Electron transfer is often associated with the conformational changes. For organic ion-radicals the inner reorganization energies remain modest, allowing a fast passage between the different conformations during the electron transfer (e.g., see Bellec et al. 2000).

Let us consider molecular switches based on intramolecular electronic transition. Generally, transfer of energy or an electron within a molecule proceeds in femtoseconds. The aim is to produce molecular electronic devices that respond equally rapidly. Molecular switches that employ optically controlled, reversible electron-transfer reactions sometimes bring both speed and photostability advantages over molecular switches which are usually based on photochemical changes in their molecular structure. Important examples are the molecular switches depicted in Scheme 8.3 (Debreczeny et al. 1996).

The switching compounds exemplified by Scheme 8.3 work as a two-pulse electronic pump. In toluene, the first laser pulse (at 416 nm) instantly produces a one-electron shift, forming the amine cation-radical part and di-imide anion-radical part. The second laser pulse (at 480 nm) rapidly (3 ns) switches the ion-radical separated state back to the initial form. Substitution of the methoxy group for the methyl group in the benzene bridge represents a useful expansion of the switch-molecule series. The dimethoxy derivative exhibits increased rates of charge separation and recombination relative to those of the corresponding dimethyl substituted bridge. The effect is also particularly strong in toluene (Miller et al. 2000). The molecular arrays described, provide a basis for the design of molecular electronic devices.

Based on the assembly of highly fluorescent acceptor perylene-3,4:9,10-bis (dicarboximide) with easily cation-radical forming tetrathiafulvalene (TTF), Leroy-Lhez et al. (2005) constructed a new reversible fluorescent redox-dependent molecular system. They synthesized this system by the esterification of two building blocks depicted in Scheme 8.4. The physical mixture of both components (before esterification) displays fluorescence only from the perylene counterpart. The chemical “mixture,” that is, the ester loses fluorescence quantitatively (~99.7%). This loss of fluorescence is the result of a photoinduced electron transfer from the thiafulvalene fragment (a strong donor) to the perylene-amide moiety (a pronounced acceptor). However, in the ester considered, the thiafulvalene fragment keeps the possibility to be selectively transferred into the cation-radical state at low anodic potentials. Because of the transformation into the cation-radical state, the fulvalene cannot



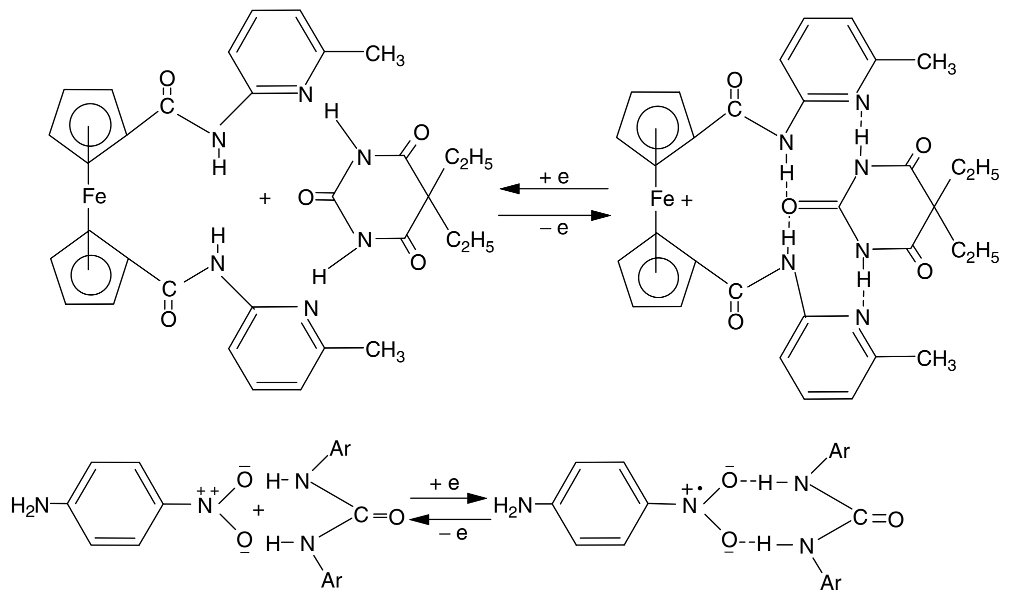
SCHEME 8.4

participate in electron donation to its acceptor neighbor anymore, and the perylene fluorescence emission is restored. We deal with an effective molecular switch of the fluorescent type.

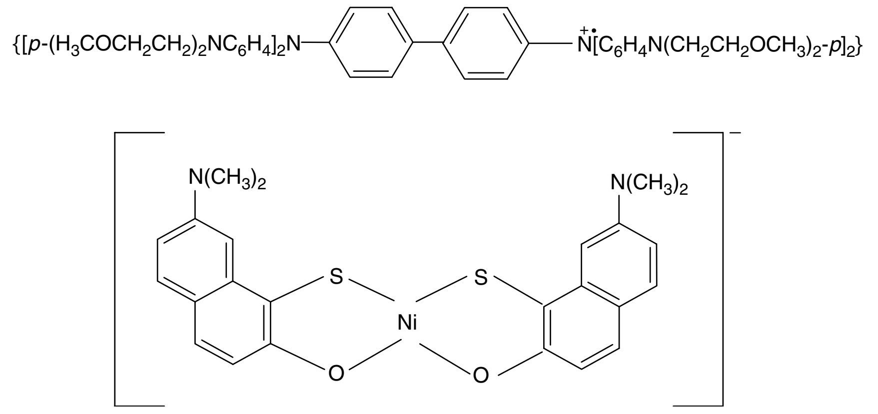
Electro-optical modulators are other examples whose efficiency is enhanced in the presence of ion-radicals. These devices are based on the sandwich-type electrode structures containing organic layers as the electron/hole-injecting layers at the interface between the electrode and the emitter layer. The presence of ion-radicals lowers the barrier height for the electron or hole injection. Anion-radicals (e.g., anion-radicals from 4,7-diphenyl-1,10-phenanthroline—Kido and Matsumoto 1998; from tetra (arylethynyl) cyclooctatetraenes—Lu et al. 2000; from bis (1-octylamino) perylene-3,4:9,10-bis (dicarboximide)s—Ahrens et al. 2006) or cation-radicals (e.g., cation-radicals from α-sexithienyl—Kurata et al. 1998; 1,1-diphenyl-2-[phenyl-4-*N*,*N*-*di*(4′-methylphenyl)] ethylene—Umeda et al. 1990, 2000), all of them are electron or hole carriers.

As mentioned earlier in Chapter 5, there are ion-radicals capable of forming hydrogen-bond complexes with neutral molecules. Such complexation significantly changes the redox potential comparatively to that of an initial depolarizer. Of most importance is that the formation of ion-radicals is a reversible process. In other words, the redox-switched effect operates in this host–guest systems. Scheme 8.5 illustrates the effect realized in the systems of ferrocene/ferrocenium (Westwood et al. 2004) and of nitrobenzene/the nitrobenzene anion-radical (Bu et al. 2005).

Scheme 8.5 demonstrates a very strong, reversible, redox-dependent interaction between depolarizers and urea analogs in aprotic solvents. There is essentially no interaction between these solutes when they exist in uncharged states. However, redox reaction creates a very strong interaction with urea analogs due to strong hydrogen bonding. This results in a new, on/off organic redox switch that compares very favorably to those previously proposed. The systems considered could be practically useful for creation of more elaborative receptors with greater selectivity and functionality.



SCHEME 8.5

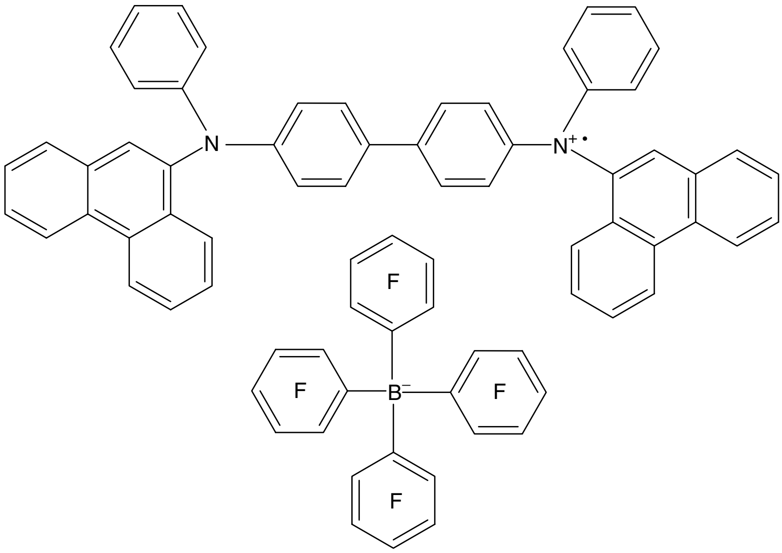


SCHEME 8.6

8.2.2 Cation-Radicals of Triarylamines in Optical-Recording Media

Organic dyes of a particular structure change their physical properties on irradiation with light of a relatively long wavelength. Such dyes can be used for recording layers. If a polymethine dye, which exhibits appropriate sensitivity to exposure by a laser beam, is used in a thin film, this film forms an optical recording medium that permits both laser recording and reflecting reading.

In the recording layer, however, the organic dye tends to deteriorate after repeated irradiation with reproduction light, and the reproduction properties of the optical recording medium, thereby, also deteriorate. A very high voltage is forced to use in the devices working in the regime of electroluminescence. As claimed (Mihara et al. 1997), it is possible to improve significantly the light resistance of the organic dye used by combining the organic dye and a nitrogen-containing cation-radical salt with metal complex anion. One of such cation-radical salts is shown in Scheme 8.6.



SCHEME 8.7

The patent by Mihara et al. (1997) enumerates many representatives of cation-radical salts, dyes, and polymers for layers. The problem of the salt solubility is a bottleneck in this kind of application. It is the salt of the metal complex anion and the cation-radical of a triarylamine that easily dissolves in typically used organic solvents that do not affect plastics (the base of a layer). At the same time, the productivity of optical recording media is significantly increased. It is possible to obtain an optical recording medium exhibiting excellent preservation stability under conditions of high temperature and high humidity. It is also possible to obtain an optical recording medium having a distinct threshold value for laser power without degrading the high reflectance and high sensitivity of the organic dye used. The mechanism of cation-radical action remains unclear. Probably, it can be caused by redox activity of cation-radical additives.

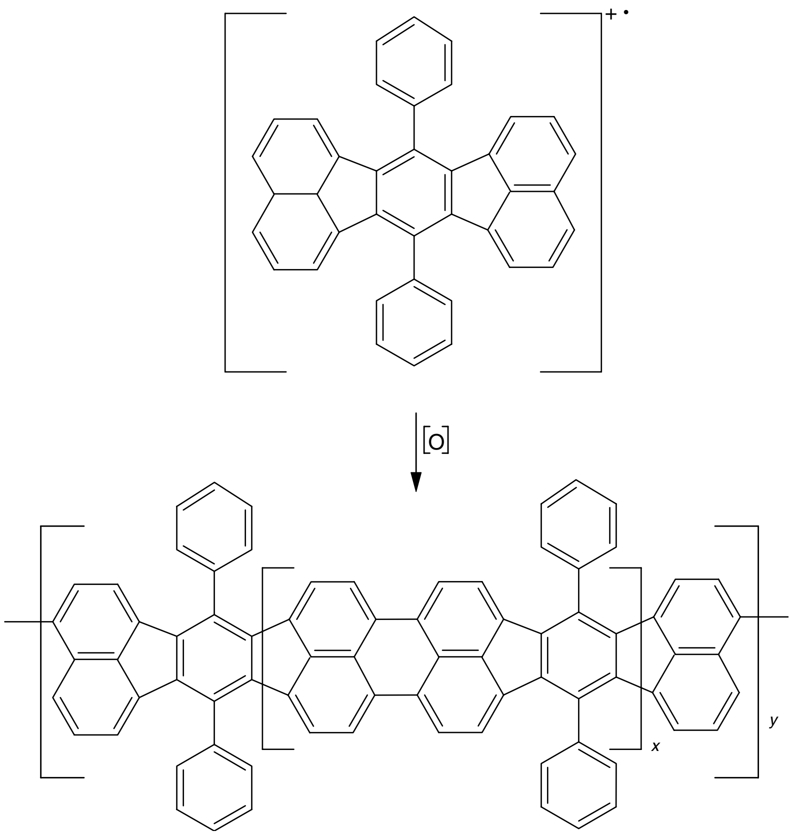
The second claim by Iida et al. (2007) refers to a composite of an organic electroluminescence device comprising a luminescent material and triarylamine cation-radicals that open a possibility to use a lowered working voltage and to enhance the device durability. Scheme 8.7 represents one of the examples from this patent.

8.2.3 Ladder Polymerization of Fluoranthene-Based Cation-Radicals as Route to Electrochromic Materials

Fluoranthene derivatives transform into cation-radicals upon one-electron oxidation. These species are not stable and quickly undergo further oxidation. For example, 7,14-diphenylacenaphtho [1,2-k] fluoranthene gives a ladder polymer according to Scheme 8.8 (Debad and Bard 1998).

As a result, an insoluble transparent blue polymer film forms on the electrode. Electrochemical oxidation of the film in acetonitrile initiates a rapid color change from blue to pale gray, while reduction to the first or second cathodic waves causes the film to become pale green or orange, respectively. These electrochromic effects are stable and reversible when air and water are excluded, even after 30,000 reduction cycles. The material has potential uses in electrochromic or electroluminescent devices.

Stable ladder oligosilanes are also of interest. The potassium metal reduction of the neutral ladder oligosilanes containing 6–12 silicon atoms fully substituted by isopropyl groups leads to the formation of corresponding anion-radicals that are highly stable at room temperature (Kyushin et al. 2000). These silanes can be used as electric switchers.



SCHEME 8.8

8.3 ORGANIC METALS

Organic ion-radicals exist as salts with counterions. As seen in the preceding chapters, neutral molecules with strong acceptor/donor properties form rather stable ion-radical salts. Under certain conditions (see later), components of an ion-radical salt pack up in a crystal lattice in a special manner. Different ion-radical parts (cations and anions separately) line up one over the other in the form of endlessly long, practically linear one-dimensional (1-D), piles-chains. These piles-chains form a crystal.

Overlapping of the highest occupied molecular orbitals of organic ion-radicals (in the layers) results in the formation of a wide energy band. Electron delocalization occurs in the framework not only of one molecular contour but also in an ensemble of many molecules. As a consequence, electrons shift along piles-chains of organic ions and electric conductivity emerges. Naturally, this conductivity is large along chain axes and insignificantly small along all other directions. The electric conductivity of such organic materials makes them related to metals. This was the reason why conductive ion-radical salts were named "organic metals" or "organic conductors." They resemble metals not only with respect to electric conductivity but also to dependence of the conductivity on temperature, to some extent. Higher the temperature, lower is the conductivity. This is not surprising, since at higher temperatures all particles move more rapidly and are arranged in a less orderly fashion.

Some organic conductors can become superconductors under certain conditions. *Superconductivity* is the disappearance of electrical impedance that allows electric current to flow without any loss of energy. Organic metals were reviewed in many sources (see, e.g., Khideckel' and Zhilyaeva

1978, Andre et al. 1976, Farges 1994 as well as Grossel and Weston 1994, and, more recently, Shibaeva and Yagubskii 2004 or Shibaeva et al. 2006).

The most prospective donors are those that have ionization potentials of $I_D \leq 6.6$ eV. Acceptors with electron affinities of $E_A \geq 2.6$ eV are suitable. When $I_d - E_A \leq 4$ eV, donor–acceptor interaction leads to strong molecular complexes with a charge-transfer degree more than 0.5. Donor–acceptor charge transfer often results in the formation of ion-radical salts having metallic conductivity. In terms of charge-transfer degree, ion-radical salts are characterized with the values ≥0.7.

One important condition for achieving the metallic state is the maximal close mutual disposition of components of an ion-radical salt in a crystal (within and between stacks of cation and anion components). For charge-transfer or electron-transfer interaction, the species contacts must be equal or shorter than van der Waals distances (Le Magueres et al. 2000). Such short contact means maximal density in the components' packing, their intense interaction, and the transference of electrons along a conductive chain. The electron (charge) transfer can, in principle, be implicated in the interstack hydrogen bonds, and a charge-transfer increase strengthens these hydrogen bonds (Oison et al. 2001). The last phenomenon has never been considered up to the Oison's work of 2001. It deserves some explanation in greater detail.

In each molecule, the molecular orbitals are coupled through repulsive electron–electron interactions. A charge variation in the frontier molecular orbital is concerted. It leads to dilation or contraction of the electronic cloud formed by lower molecular orbitals, essentially in the molecular plane. This leaves an excess of charges of the same sign on the periphery of each molecule and increases the reactivity of the molecules occurring in their plane. This effect is enhanced in the crystals by the mutual influences of neighboring molecules. Hence the effects along π- and hydrogen-bond chains are intimately coupled in the charge (electron) movement with respect to molecular ensembles.

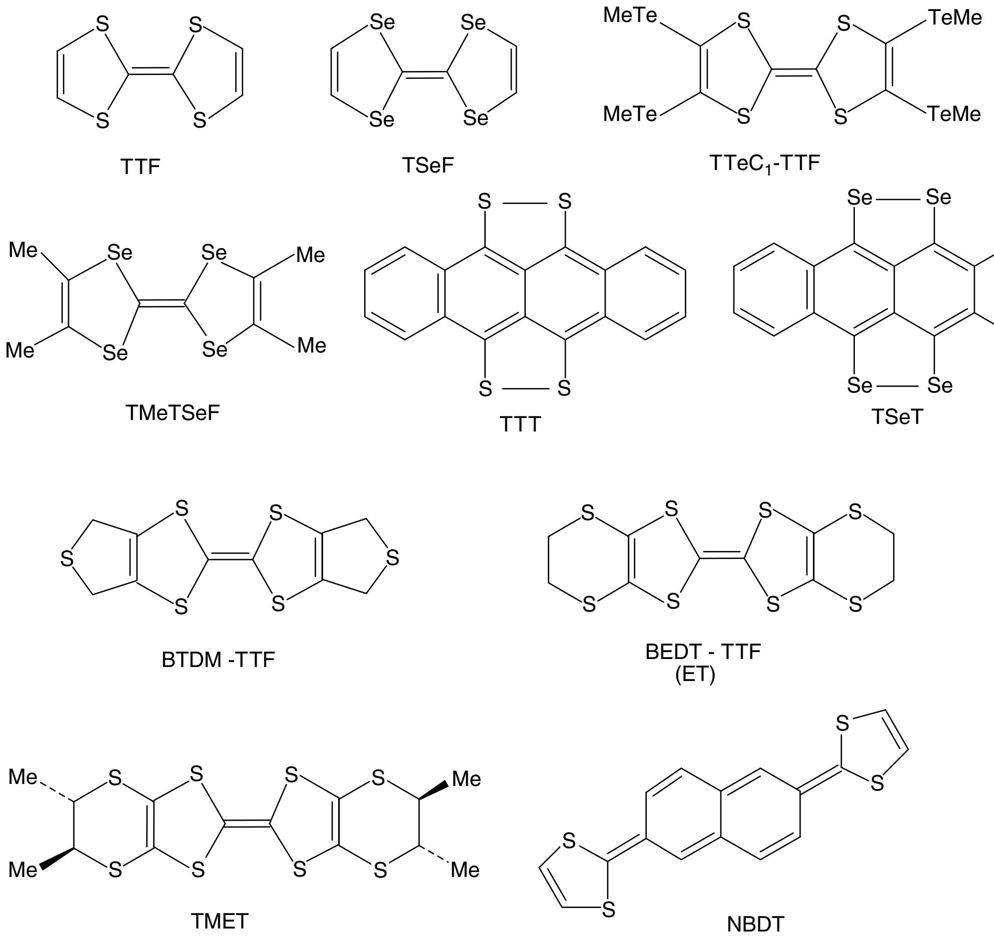
The following compounds are the most popular donors for organic metals (see Scheme 8.9): TTF, tetraselenafulvalene (TSeF), tetrathiatetracene (TTT), tetraselenatetracene (TSeT), tetramethyl tetraselenafulvalene (TMeTSeF), bis(thiadimethylene) tetrathiafulvalene (BTDM-TTF), bis(ethylenedithia) tetrathiafulvalene (BEDT TTF or ET), tetrakis(methyltelluro) tetrathiafulvalene ($TTeC_1$-TTF), tetramethylbis(ethylenedithia) tetrathiafulvalene (TMET), 2,2′-(2,6-naphthalenediylydene) bis(1,3-dithiole) (NBDT). All the abbreviations are those used in the current literature.

Organic donors must exhibit not only a desirable electron-donating ability, but also strong intermolecular interactions. The latter property, which permits the delocalization of an unpaired electron along the uniform stack, is achieved by increasing the number of relatively voluminous heteroatoms. To date, it has been shown that multisulfur heterocycles and their selena and tellura analogs are the most promising candidates as components for organic metals. The introduction of chalcogen atoms in organic unsaturated derivatives decreases their ionization potential and stabilizes the corresponding cation-radicals. The relative polarization of chalcogens is, therefore, an important factor. Close contacts between chalcogen atoms arising from ring-over-bond overlap in the crystal stacks provide the framework for 1-D intermolecular delocalization of unpaired electrons. Naturally, larger the atomic size of a chalcogen, closer the contact is possible.

Sometimes, hydrogen bond also enhances intermolecular interactions and spin delocalization. Thus, TTF bearing imidazolyl (TTF-IM) reacts with *p*-chloranil (CA) and forms a charge-transfer complex. In this complex, the hydrogen bonding occurs between the imidazolyl N–H fragment of TTF-IM and C=O groups of CA. The polarizability of hydrogen bonds controls the TTF-IM to be oxidized and CA to be reduced. After electrocrystallization, a cation-radical salt with iodide anion was prepared. The salt is highly ordered in its crystal state and acquires sufficiently high electric conductivity (Murata et al. 2007).

It should be noticed that on-site electrostatic repulsion is also important for designing organic conductor constituents. Extension of π-electron conjugation is one of the most effective methods to reduce this repulsion. Hexafluorophosphate salt of the bis(1,3-dithiole) cation-radical salt

Donor components for organic metals

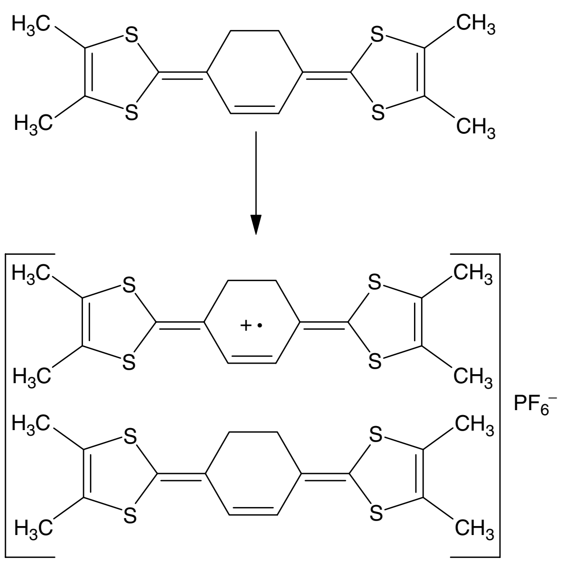


SCHEME 8.9

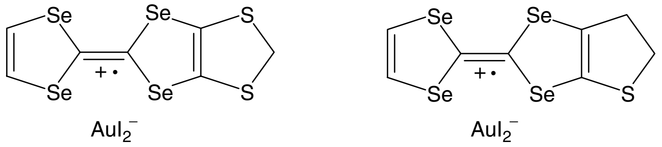
containing cyclohexene unit is a prominent example (see Scheme 8.10). The salt exhibits good conductivity of $1 \times 10\ \Omega^{-1} \cdot cm^{-1}$ at room temperature (Yamashita et al. 2002). (The unit of conductance is denoted as Ω^{-1}, or ohm^{-1}, or even mho, but mostly as S, i.e., Siemens [$1\ S = 1\ \Omega^{-1}$].)

BTDM-TTF is one of the most powerful donors of the TTF class. Alkylthio-substitution, such as in BEDT-TTF (ET), leads to a slight reduction in its electron-donor ability. Nevertheless, salts of this cation-radical with tetracyanoquinodimethide (TCNQ) and its derivatives show significantly higher conductivity (by ca. 10^2–10^3) than the analogous BTDM-TTF salts (Grossel and Weston 1994). This reflects some enhancement of intra and interstack interactions produced by the sulfur atoms at the edges of the donor skeleton.

Thus, the ion-radical salt of BTDM-TTF (ET) with TCNQ has a high conductivity $1.3 \times 10^2\ \Omega^{-1} \cdot cm^{-1}$ at room temperature with metallic behavior down to 26 K (Rovira et al. 1994). The striking observation was made that the nature and molecular size of donor or acceptor have no substantial effect on the molecular distance within a stack (from 0.32 to 0.35 nm). Meanwhile, increase in the volume of a heteroatom leads to improvement in the intermolecular interactions within given stacks. The enhanced intermolecular interactions were indeed observed with the substitution of selenium for sulfur.



SCHEME 8.10



SCHEME 8.11

The aforementioned orbital dispersion is more pronounced in the selenium-containing representatives. This arises from the more extensive overlap properties of selenium (Beer et al. 2001).

Whereas various organic salts of tetramethyltetrathiafulvalene never exhibited superconductivity, those of tetramethyltetraselenatetrathiafulvalene, known as the Bechgaard salts, were the first organic superconductors discovered (Jerome et al. 1980). The selena analog of BEDT-TTF has been synthesized (Lee et al. 1983). However, this compound appeared to have very limited solubility, to the extent that its oxidation potential could not be determined. In general, the solubility problem implies severe limitations in choosing proper components for organic metals. (One of the most attractive properties of organic metals is their ability to form thin films from solutions—films that have lightweight and desired profile.)

Takimiya et al. (2001, 2003, 2006) have synthesized methylenedithiotetraselenafulvalene (MDT-TSeF) and ethylenethiotetraselenafulvalene (ET-TSeF), which were found to be soluble in organic solvents. Using anodic electrolysis supported by Bu_4NAuI_2 in ethanol–chlorobenzene solution, the authors have obtained diiodoaurate cation-radical salts of the donors. The formulas of the salts are depicted in Scheme 8.11. At room temperature, both salts showed very high conductivities of 2×10^3 and 1.6×10^3 $\Omega^{-1} \cdot cm^{-1}$, respectively. However, these salts differ with respect to superconductivity: At ambient pressure, (MDT-TSeF)–AuI_2 underwent a superconducting transition at 4.5 K, whereas (ET-TSeF)–AuI_2 did not show superconducting transition at 1.8 K. X-ray structural analysis revealed that the cation-radical part of (MDT-TSeF)–AuI_2 crystal is packed in a perfect order. On contrary, the cation-radical part of (ET-TSeF)–AuI_2 crystalline salt is packed not so orderly. As shown in Scheme 8.11, these two salts differ in their molecular symmetry. The presence of two opposite sulfur atoms in the fused five-membered ring of (MDT-TSeF)–AuI_2 provides the salt with C_2 symmetry. This is a condition of the superconductivity effect observed.

Another important way to increase the intermolecular interactions is to use the effect of "molecular fastener." This effect has been observed in tetrakis(alkylthio)tetrathiafulvalenes (the alkyl groups were longer than C_8). A relatively high conductivity was observed even in neutral donors (Inokuchi et al. 1986). This phenomenon was explained through the enhancement of intermolecular contacts induced by van der Waals interactions of the alkyl side chains. Importantly, a high intrinsic conductivity has been observed also for tetrakis(methyltelluro)tetrathiafulvalene. In this case, tellurium atoms were claimed to play the role of molecular fasteners (Inokuchi et al. 1987). The authors explain this effect in terms of the manner of molecular packing and stacking within the crystal. The central skeleton of this compound, the tetratelluro-tetrathiafulvalene moiety ($C_6Te_4S_4$) is almost planar and is regularly stacked in the form of column. Along the stacking axis, tellurium atoms in neighboring columns come close to each other and form zigzag columns. The distance between these Te atoms is 0.364 nm, which is significantly shorter than van der Waals distance (0.412 nm). The zigzag chalcogen chains are supposedly formed from quasi-covalent bonds (Inokuchi et al. 1987).

Compared to usual organic conductors, the molecular conductors based on the tellurium-containing π donors show a very strong tendency to form a 3-D network mediated by tellurium atoms. Owing to the strong Te···Te network, the anions (which are counterions to the cation-radicals) contribute little to the architecture of crystal structures and are located fairly randomly in the channels that are formed by the organic cation-radicals. Such a peculiarity is useful for electric conductivity. For example, the bis(peri-ditellurium) bridged *sym*-tetramethylnaphthalene cation-radical salt with thiocyanate anion forms 1-D columns and constructs a 3-D network between the columns through the intermolecular contacts between the protruded tellurium atoms. This salt is highly conductive (590 $\Omega^{-1} \cdot cm^{-1}$ at room temperature) and maintains a metallic behavior down to 4.2 K (Fujiwara et al. 2005).

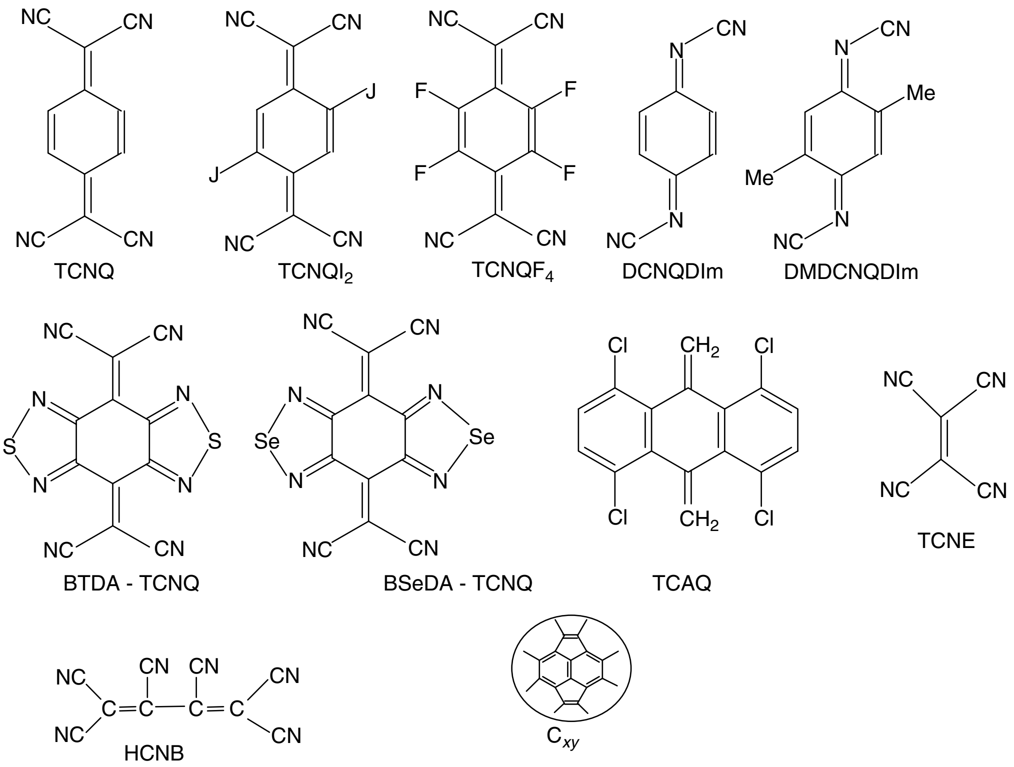
As acceptors for organic metals, the following compounds are widely used (see Scheme 8.12: TCNQ, tetracyanoperfluoroquinodimethide [$TCNQF_4$], tetracyano-2,5-diiodoquinodimethide [$TCNQI_2$], *N,N*-dicyanoquinodiimine [DCNQDIm], 2,5-dimethyl-*N,N*-dicyanoquinodiimine [DMDCNQDIm], tetracyanoethylene [TCNE], hexacyanobutadiene [HCNB], bis[thiadiazole] tetracyanoquinodimethide [BDTA-TCNQ], bis[selenadiazole] tetracyanoquinodimethide [BSeDA-TCNQ], 1,4,5,8-tetrachloro-9,10-anthraquinodimethane [TCCAQ], fullerenes [C_{xy}, e.g., C_{60} or C_{80}] and other molecules). The abbreviations used here are also generally found in the current literature.

Most organic acceptors used in the preparation of organic conducting materials belong to a class of polycyano compounds. The reasons are quite obvious if the unique properties of the cyano group are taken into account. It is a very strong acceptor and has a very small size with minimal steric strain. (Note the rod-shaped form of C≡N group.)

The TCNQ anion-radical also has high thermal stability. Ring substitution in the six-membered ring in TCNQ allows modification of the properties of corresponding ion-radicals. Grossel and Weston (1994) pointedly mention that incorporation of heteroatoms or heterocyclic rings into the TCNQ skeleton leads to greater intra- and interstack interaction. This increases dimensionality, stabilizes conductivity, and enhances the metallic state. Selective deuteration of dimethyl-TCNQ is also a way to change its properties in this sense. Interestingly, selective deuteration of the methyl groups plays a much greater role than deuteration of the ring protons (Grossel and Weston 1994).

In creating an organic metal, one should avoid transformation of a conductor into a dielectric. Such a transformation can occur with decreasing temperature. The conductivity of many organic metals grows upon cooling from −70 to −100°C, after that it drops abruptly. Organic metals turn into insulators and cease conducting electric current. The cause is Peierls instability or Peierls distortion, which is typical for 1-D systems. According to the so-called Peierls theorem for long chains, irregular domains are preferentially stable. At certain critical temperatures, ion chains become sectioned. At the ends of each section, the distances between ions are shortened, while those between the sections are lengthened. This creates high barriers to electron jumps along the chain and abolishes its electric conductivity.

Acceptor components for organic metals



SCHEME 8.12

In this sense, the salt of TTF cation-radical with the TCNQ anion-radical is an outstanding example. TCNQ being a strong oxidant, transforms TTF into the cation-radical. In this cation-radical, one ring acquires 6-π (aromatic) electron structure bearing the single-unit positive charge, whereas the other ring puts up with an unpaired (delocalized) electron. Both rings are connected through the ethylene bond between them so that the electron state of each ring can be changed, reversibly. In other words, TTF cation-radical is characterized by high electron mobility. Aromatization provides the thermodynamic force for TTF to act as an electron donor. Furthermore, aromatization causes a change in TTF molecular structure from puckered to planar in the oxidized cation-radical state. This conformational change is advantageous to sulfur–sulfur contacts in a crystal pack to achieve quasi-2-D electric conductivity. The electric conductivity of TTF-TCNQ salt is equal to 10^3–10^4 $\Omega^{-1} \cdot cm^{-1}$ in the temperature interval from −170 to +40°C (Khideckel' and Zhilyaeva 1978) or 10^5 $\Omega^{-1} \cdot cm^{-1}$ at −213°C (Shibaeva et al. 2006). By comparison, metallic copper has an electric conductivity of 10^6 $\Omega^{-1} \cdot cm^{-1}$ at 27°C.

Several attempts were undertaken to convert organic metals into superconductors. The first organic superconductor was $(TMeTSeF)_2^{+\bullet}PF_6^-$. The transformation took place at 0.9 K and 1 hPa. Substitution of ClO_4^- for PF_6^- led to the formation of a superconductor at normal pressure and temperature of 1.2 K (Jerome et al. 1980). In addition, salt of ET cation-radical with iodide was prepared (Kaminskii et al. 1984). It also showed superconductivity at normal pressure. Superconductivity temperatures increased up to 7 K with iodine contents. It was established that a semiconducting sample of $(ET)_2^{+\bullet}I_3^-$ (the so-called α-phase) transformed into the superconducting β-phase upon heating (Baram et al. 1986). Currently, there are about a hundred of known organic superconductors, including the compounds based on Buckminsterfullerene C_{60}. Most of them contain ET cation-radical component (Ishiguro et al. 1998).

Fullerenes (C_{xy}) have internal cavities, which can act as containers for metal atoms. The metal reduces C_{xy} and is trapped in a fullerene cage (Saalfrank 1996). For example, Buckminsterfullerene C_{60} can react with two potassium atoms producing a dianion–diradical that is a triplet in its ground state. Alkali metal salts of Buckminsterfullerene C_{60} possess the highest superconductivity transition temperatures (T_C) to date for organic materials, for example, K_3C_{60} with $T_C = 19$ K, Rb_3C_{60} with $T_C = 29$ K, and Cs_2RbC_{60} with $T_C = 33$ K (Haddon et al. 1992). Localization of the unpaired electrons at definite sites of the fullerene internal sphere is a promising property of these alkali metal salts.

The results were promising, but did not last long because of the discovery of inorganic ceramics. The ceramics displayed superconductivity without any cooling (Vanderah 1992). Nevertheless, organic metal and superconductors have their advantages, and investigation is carried out in this direction.

As starting materials for organic metals, organic substances must correspond to several general requirements. Namely, both acceptors and donors must form redox systems, with the participation of not only ion-radicals but also double-charged ions, $A + e \rightarrow A^{-\bullet} + e \rightarrow A^{2-}$ or $D - e \rightarrow D^{+\bullet} - e \rightarrow D^{2+}$. Ion-radicals play a role as mediators in these two-electron transfers. Each one-electron step achieves a maximal rate, and both rate constants become closer. Electrostatic repulsion of positive (or negative) charges makes the double-charged ion formation difficult. Therefore, donors (or acceptors) are preferable for which some possibility exists to disperse the charge. Extension of the π system reduces intramolecular coulombic repulsion in the dianion state. Electron donor (or electron acceptor) substituents should be located at diametrically opposite sites of the molecule. Examples are 11,11,12,12-tetracyano-9,10-anthraquinodimethide, TCNQ, DCNQI, and tetracyanobenzene. In TCNQ, the cyano groups are in the most remote (face-to-face) positions. This diminishes coulombic repulsion of two surplus electrons in the dianion and, consequently, facilitates an electron transfer along the conductive chain. In tetracyanobenzene, the ring substituents are close to each other. The (anion-radical)-to-(dianion) transformation energy appears to be larger than that for TCNQ. Tetracyanobenzene forms only dielectric salts. In contrast, TCNQ is able to give salts with high conductivity.

Donors and acceptors should acquire and keep a planar or almost planar structure in an ion-radical state. This ensures the maximal density in a crystal lattice and the space monotony in the arrangement of stacks.

This requirement to planarity is important but not very strict. The salt $[(TTF)^{+\bullet} (TCNQ)^{-\bullet}]$ is an example. It possesses metallic conductivity. However, its fulvalene rings are not strictly coplanar and the cyano groups are, to a certain degree, bent in respect of the quinone ring. Moreover, one organic metal has been prepared on the basis of the principally nonplanar chiral ion-radical $(TMET)_2^{+\bullet} PF_6^-$. Its conductivity is equal to 5 $\Omega^{-1} \cdot cm^{-1}$ at ambient conditions (Wallis et al. 1986).

There is a rule that donor and acceptor components for a planned ion-radical salt should have more or less symmetrical molecular geometry. However, if substituents are not so bulky, they can be located unsymmetrically without detriment to conductivity (Tatemitsu et al. 1985). Scheme 8.11 also testifies that such a rule should be understood dialectically.

Complexation of ion-radicals with the parent molecules without formal charge is necessary to build conducting stacks of quasi-1-D organic metals. For instance, in films of the highly conducting salt $[(TTF)^{+\bullet} (TCNQ)^{-\bullet}] \cdot TCNQ$, 20–50% of the neutral TCNQ molecules are at the surface. Meanwhile, there are no neutral and, separately, charged components in a stack. In all the TCNQ molecules, bond lengths are equal and are involved in complexation (Khideckel' and Zhilyaeva 1978). In this salt, the degree of charge transfer between the TTF donor and the TCNQ acceptor is different from unity and equal to 0.59 (Van Duyne et al. 1986, Tanaka et al. 1986). In the case of 2,5-dimethyltetracyanoquinodimethide (DMTCNQ) as the donor, $[Me_2N^+ (DMTCNQ)^{-\bullet}] \cdot 1/2DMTCNQ$ exhibits a conductivity of 1.5 $\Omega^{-1} \cdot cm^{-1}$, and $[Me_4P^+ (DMTCNQ)^{-\bullet}] \cdot 1/2DMTCNQ$ shows a conductivity of 3.7 $\Omega^{-1} \cdot cm^{-1}$ (both magnitudes at 280–310 K). Besides this high electric conductivity, the salts exhibit ferromagnetic behavior. These mixed salts provide the important example of a

molecular organic system, which can exhibit both electrical conductivity and ferromagnetic behavior at room temperature (Sugimoto et al. 1998). Obviously, for these mixed salts a carrier s/p electron and a local s/p spin coexists, and this coexistence is essential for a high electrical conductivity and ferromagnetic behavior, respectively.

All these data verify that in real systems, the rate of electron transfer between components of a conductive chain is high. There are states of a mixed valence. Enhanced electric conductivity and other unusual physical properties are widespread among those inorganic or coordination compounds that contain metals in "intermediate"-valence states. In cases of organic metals, nonstoichiometric donor/acceptor ratios provide even better results. For example, the salt of $(TTF)_1\,(Br)_{0.7}$ composition displays an electric conductivity of $2 \times 10^2\ \Omega^{-1} \cdot cm^{-1}$, while $(TTF)_1(Br)_1$ salt does not conduct electricity at all (Khideckel' and Zhilyaeva 1978).

Increasing the polarizability of components facilitates the collective shift of electrons and the stabilization of the material's metallic state. Thus, substituting selenium for sulfur (changing from TTF to TSeF) allows one to obtain organic metals that do not transform into dielectrics up to very low temperatures. Chloride and bromide of tetraselenatetracene, $(TSeT)_2(Cl)_1$ and $(TSeT)_2(Br)_{1,}$ have the same conductivity at room or low temperatures.

In chemistry of organic metals, preparative methods differ from those in organic ion-radical chemistry, the main difference being the necessity of constructing conductive stacks. Stacks must be built with components that are in the mixed-valence state. The reviews cited above describe these methods in details. The majority of ion-radical salts having structures with regular endless chains are obtained by means of direct interaction of donors and acceptors in solutions. To achieve these mixed-valence compounds, nonstoichiometric relations of components are employed. The rates of cooling of the resulting mixture are very important.

For example, at a ratio of molecular iodine to tetrathiatetracene (TTT) of 1:2, mixtures of iodides $(TTT)_1(I)_1$ and $(TTT)_2(I)_3$ can be obtained on fast cooling. Slow cooling of the same component mixture in the same proportion leads to the single product $(TTT)_2(I)_3$. The latter is just the product that possesses metallic properties. Sometimes, even at nonstoichiometric ratio, salts of the 1:1 composition are formed. Interaction between TTF and TCNQ can be exemplified. To obtain the 2:1 composition, an indirect synthesis is appropriate. The synthesis is based on an exchange reaction of the following type:

$$(TTF)_8(BF_4)_5 + (Bu_4N)_2(TCNQ)_1 \rightarrow (Bu_4N)(BF_4) + (TTF)_2(TCNQ)_1$$

In individual cases, it is expedient to perform the interaction of a donor and an acceptor in gaseous phase by means of joint vacuum sublimation of the components. Such a method was employed in the case of $(TTT)(TCNQ)_2$. In this example, solvent admixtures are absolutely absent in the conductive material.

By means of this vapor diffusion method, superconducting films of C_{60} compounds with alkali metals (M_3C_{60}) were first prepared at AT&T Bell Laboratories (Haddon et al. 1991). Meanwhile, pure K_3C_{60} can be prepared by mixing powdered potassium metal and C_{60} in toluene (Wang et al. 1991). The already mentioned alkali anion-radical salts of the KC_{60} type were formulated as product of intercalation of C_{60} fullerene by an alkali metal in organic solution. It would be interesting to perform a reaction between C_{60} fullerene and 1 equivalent of finely powdered potassium in the THF solution containing 18-crown-6 ether. In this case, the resulting potassium cation would be bound by the crown and removed into the outer sphere, whereas an excessive electron would occur inside fullerene cave. It may enhance the metallic conductivity of the anion-radical part. Such a construction is realized when carborane reacts with 1 equivalent of sodium in the THF solution containing 18-crown-6-ether (Fu et al. 2007).

The physical properties of crystals depend on admixtures; this is common knowledge. The admixtures can be present in a starting solution. Solvent molecules included in a crystal during its formation should be considered a contamination. In this sense, the highest attention should be

paid both to the purification of the starting materials and to the improvement in crystal-growing methods. The main purpose is to obtain a crystal lattice with minimal defects. For the salt $[(TTF)^{+\bullet}$ $(TCNQ)^{-\bullet}]$ mentioned earlier, electric conductivity depends more on the lattice defects than on the degrees of purity that can usually be achieved by chemical syntheses. At the same time, the indices of magnetic susceptibility, heat absorption capacity, and paramagnetism are subjects to influence of admixtures. In the sense of molecular properties, admixtures (disturbing the laws of continuum) lower the appropriate indices.

As a rule, recrystallization cannot be used for the purification of organic metals. Recrystallization is usually performed under definite thermal influence and leads to impure, "imperfect" crystals. Ion-radical salts are thermally unstable in solutions. However, a technically important goal to fabricate molecular wire requires well-controlled recrystallization. Ueda et al. (2006) prepared molecular wires of $[(NMP)^{+}$ $(TCNQ)^{-\bullet}]$ and $[(Et_4N)^{+}$ $(TCNQ)^{-\bullet}]$ by controlling the solvent evaporation rate from acetone solution. Here NMP and Et_4N stands for *N*-methylphenazinium and $(Et_4)N^{+}$– for tetraethylammonium, respectively. Microscopic images showed that changing the evaporation rate from 167 to 1.7 μL/min increases the stripe size from 35 nm to 1 μm. Comparison of the IR spectra and X-ray diffraction pictures with those of the corresponding single crystals clearly indicated that the wires have the same crystallinity as the single crystals. Conducting path will supposedly align to the preferentially grown direction.

The direct donor-to-acceptor interaction is the best way to limit chemical impurities. In this case, the reaction mixture contains minimal amounts of substances that are not included in the structure of a given ion-radical salt. The oxidation of donors in the presence of anions or ion exchange usually results in the formation of less pure crystals.

The correct choice of the method for growing crystals is very important. Slow crystallization of a reaction mixture at a fixed diffusion rate can be achieved by means of a H-shaped tube. Separate flasks with the solutions of a donor and an acceptor are joined by the H-shaped overturned tube. The tube is filled with a solvent. A donor and an acceptor slowly diffuse together, react, and form a crystalline product. As a rule, this process proceeds at room temperature. The method leads to the most perfect crystals of an ion-radical salt.

In the H-shaped tube, all processes take place in a slow, controlled way. One simple modification consists of separating the two halves of the H-shaped tube with a fitted glass disk (medium, fine, or ultrafine porous) to slowdown the diffusion. Another modification involves diffusion inside the reaction solvent containing a polymer. In this case, diffusion is retarded due to an increase of the solution viscosity (Scott et al. 1974, Berg et al. 1976). Sometimes, the synthesis of ion-radical salts is conducted ultrasonically if the starting materials are insoluble in the desired solvents (see, e.g., Neilands et al. 1997).

Electrocrystallization is also an effective method. It is used for the preparation of organic metal containing an organic ion-radical and an inorganic counterion. The technique gives rise to high-quality organic molecular conductors and superconductors. In this approach, donors or acceptors are oxidized or reduced electrochemically to form cation-radicals or anion-radicals. Crystal formation takes place at the working electrode when the radical cations/anions combine with suitable counterions that are furnished by the supporting electrolyte. Moderately polar organic solvents are employed generally (THF, methylene chloride, chlorobenzene, benzonitrile). For instance, electrochemical oxidation of DCNQIm and $CuBr_2$ leads to the formation of black crystals having the composition DCNQIm · 2Cu. Electric conductivity of this material reaches even $10^3\ \Omega^{-1} \cdot cm^{-1}$ at room temperature (Huenig et al. 1988). The crystal structure of the salt consists of segregated columns formed from the quinone imine and the copper ion in which the copper chains are surrounded by four quinone imine stacks (Aumueller et al. 1986).

Electrocrystallization can be conducted under conditions of constant current or constant voltage. Under constant-current conditions, the initial current density should be low and increased as required. Optimum current densities are usually in the range of 0.1–0.5 $\mu A\ cm^{-2}$. The influence of the current density and voltage on the sizes, quality, phase states, and stoichiometry of the crystals obtained has been discussed (Ward 1989, Faulmann et al. 1993).

Although the electrochemical method is widely employed for producing monocrystalline nonstoichiometric salts, it has some disadvantages such as long reaction times (up to several weeks) and drastic limitations imposed on solvents and the amount of the target product (a few milligrams). In contrast, the chemical approach does not suffer from these restrictions and can theoretically afford unlimited quantities of materials.

Recently, one general route was proposed that involves oxidation of the starting neutral molecule by (diacetoxyiodo)benzene in the presence of strong acids. The resulting salt is highly soluble. Thus, oxidation of TTF in acetonitrile follows this scheme (Giffard et al. 2001):

$$R_4TTF + \tfrac{1}{2}PhI(OAc)_2 + CF_3SO_3H \rightarrow (R_4TTF)^{+\bullet}CF_3SO_3^- + \tfrac{1}{2}PhI + AcOH$$

$$(R_4TTF)^{+\bullet}\,CF_3SO_3^- + nR_4TTF + Alk_4N^+X^- \rightarrow Alk_4N^+CF_3SO_3^- + (R_4TTF_{n+1})^{+\bullet}X^-$$

Stoichiometric triflates $[(R_4TTF)^{+\bullet}CF_3SO_3^-]$ are convenient precursors for the conversion depicted. On the addition of alkylammonium salt in acetonitrile solution, either stoichiometric ($n = 0$) or nonstoichiometric ($n \neq 0$) material $[(R_4TTF_{n+1})^{+\bullet}\,X^-]$ can be obtained. These targeted salts precipitate in a very pure state.

O'Mullane et al. (2007) proposed a promising modification of the reductive approach to metal-TCNQ species through photoexcitation of TCNQ in acetonitrile in the presence of a sacrificial electron donor (benzyl alcohol) and a metal salt (MX). The photochemical reaction leads to reduction of TCNQ to $(TCNQ)^{-\bullet}$. In the presence of MX, $M^+(TCNQ_{n+1})^{-\bullet}$ crystals are deposited onto a solid support with morphologies that are dependent on the metal-cation nature. Thus, $K^+(TCNQ)^{-\bullet}$ crystallizes as microrods with a random size distribution. $Cu^+(TCNQ)^-$ crystallizes as uniform microrods, and $Ag^+(TCNQ)^{-\bullet}$ as very long nanowires up to 30 μm in length and with diameters of <180 nm. The latter two salts are of particular interest for use in memory storage and switching devices (O'Mullane et al. 2007, references therein). The synthesis described was performed under normal laboratory conditions avoiding dry-box precautions. The authors pointed out that this simple technique could be employed to generate all metal-TCNQ species on any type of support.

Widening of the technical applications of organic metals depends, in many respects, on the development of methods for forming molecular structures with designed architecture. Their network structure also depends on the evaporation conditions. Thus, organic cation-radical salts can be fabricated in nanodots on appropriate supports. Diameter, height, and connectivity of nanodots depend on the evaporation process of the cast solution (Akutagawa et al. 2006). The network structure of nanodots has the potential to form nanodevices of new types. The preparation of organic metals is as much an art as a science.

As mentioned earlier, much attention was being given to the formation of ion-radical conductors in the appropriate crystalline form. Meanwhile, Ziolkovskiy et al. (2004) reported data on high conductivity at 77–300 K of the methyl-TCNQ anion-radical salts with *N*-alkylpyridinium cations that keep their conductivity after crystallization from the melted forms. The melting temperatures of the salts described are rather low and the melting proceeds without salt destruction. This feature opens a possibility to create definite, much essential constructive elements directly from the liquid phase. Importantly, these salts also possess affinity to metals due to the metal–nitrogen coordinative ability. The authors notice that such ion-radical salts are promising for use in electronics and microelectronics.

8.4 SEMICONDUCTORS

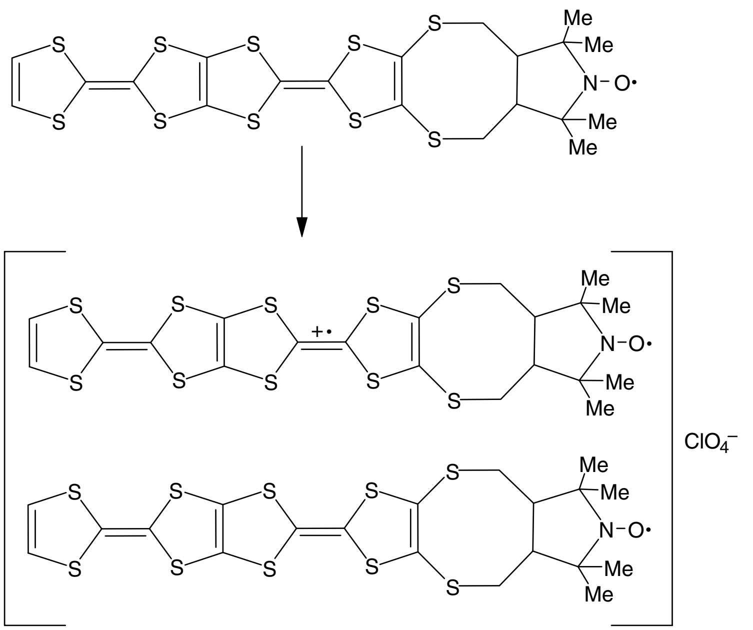
In the sense of electric conductivity, semiconductors are close to conductors but have very few free electrons. When electric resistance of metals increases with temperature, the semiconductor resistance decreases with temperature. Some of the electrons that are not free at normal temperature

become free on warming up and contribute to electric current. The resistance of a semiconductor can decrease with an increase in temperature, although this is not always the case.

For instance, 1:3 salt of the 3-[4-trimethylammonio)phenyl]-1,5-diphenyl-6-oxoverdazyl cation-radical and the nickel(1,3-dithiol-2-thione-4,5-dithiolate) anion shows the typical semiconductive properties (Mukai et al. 2004, 2005). Akutagawa et al. (2004) synthesized molecular conductor containing TCNQ and monoprotonated 1,4-diazabicyclo[2.2.2]octane ($HDABCO^+$). In the crystalline state, the 1-D dielectric (N···H···N) hydrogen bonding of the $HDABCO^+$ chains are located between the anion-radicals of $(TCNQ)^{-\bullet}$. As a matter of course, electrical conduction arises from the $(TCNQ)^{-\bullet}$ anion-radical stack, whereas the $HDABCO^+$ (N···H···N) vertical chains play only a role of insulator for dividing the electrical-conducting stacks into an individual one. However, (N···H···N) chains secure the order in dislocation of the anion-radicals in their stacks. At 100 K, $(HDABCO^+)_2\,(TCNQ^{-\bullet})_2$ (TCNQ) displays itself as a conductor. At 293 K, the material becomes a semiconductor. The warming-up destroys the hydrogen-bonding chains and this breaks the uniformity of the TCNQ stacking structure. Further increase in temperature restores electric conductivity of the anion-radical counterpart.

To obtain semiconductors with magnetic properties, Fujiwara et al. (2003) developed several donor molecules containing a stable oxyl radical moiety based on the π-extended TTF framework. The TTF framework is too small to overcome the steric hindrance of the bulky nitroxyl radical and to accomplish strong intermolecular interaction indispensable for any electric conductivity. For this reason, a larger molecule was constructed and its cation-radical perchlorate was electrochemically prepared. This salt was obtained as black microcrystals of nonstoichiomteric ratio equal to 1:0.64. Being a semiconductor, the salt also manifests magnetic properties; its structure is depicted in Scheme 8.13.

Sometimes, semiconductivity depends on the type of a structural phase that arises from synthesis. Thus, in the case of $(TCNQ)^{-\bullet}Cu^+$ the semiconducting phase is thermodynamically disfavored. To prepare this semiconductor, Harris et al. (2005) proposed to perform the reduction of TCNQ in acetonitrile at glass-carbon, gold, or platinum electrode in the presence of Cu^+. This allows the electrocrystallization of sparingly soluble TCNQCu semiconducting phase to occur by a nucleation



SCHEME 8.13

and growth mechanism that generates stable, branched needles. Electrocrystallized semiconducting TCNQCu acts as a part of the electrode, thereby effectively increasing the electrode area and favoring growth of the much required crystal phase.

8.5 ORGANIC MAGNETS

Electric conductivity of ion-radical salts arises from the mobility of their unpaired electrons. At the same time, each of the unpaired electrons possesses a magnetic moment. This small magnetic moment is associated with the electron quantum-mechanical "spin." Spin-originated magnetism as a phenomenon is described in many sources (see, e.g., monographs by Khan 1993, Bauld 1997, Itokh and Kinoshita 2001; and reviews by Miller 2000, Miller and Epstein 1994, 1995, Wudl and Thompson 1992). This section is, naturally, devoted to the organic magnets based on ion-radicals.

Any salt formed from two ion-radicals has two unpaired electrons: one belongs to the cation-radical and the other to the anion-radical. If the spins of these two electrons have an antiparallel orientation, the corresponding magnetic moments are compensating. If both spins are in parallel orientation, their magnetic moments are added together.

In parallel orientation, unpaired electrons set up according to ferromagnetic type. The antiferromagnetic type of electron setup corresponds to the antiparallel spin configuration. When the spins are coupled parallely, the material response to an applied magnetic field—termed its "magnetization"—is enhanced. When the spins are coupled in antiparallel fashion, the magnetization is suppressed. As an example of the ferromagnetic type of material, $(FeCp^{*}_2)^{+\bullet}(TCNE)^{-\bullet}$ ion-radical salt can be mentioned (Miller et al. 2001, references therein). In this structure $FeCp^{*}_2$ means decamethylferrocene.

The problem of the ferromagnetism of a solid ion-radical salt has two important points. One is ferromagnetism at the level of a salt as the molecule, which consists of two paramagnetic species. Another is ferromagnetism at the level of a solid sample formed from assemblies of the spin-bearing molecules. These molecules may contain one or more magnetic centers.

Assemblies of molecules are most often found in molecular crystals with very weak interactions between the molecular entities. They can also be found in extended systems, built from molecular or ion-radical precursors, in a way that maximizes the interactions between the precursors and, hopefully, yields bulk magnetic properties.

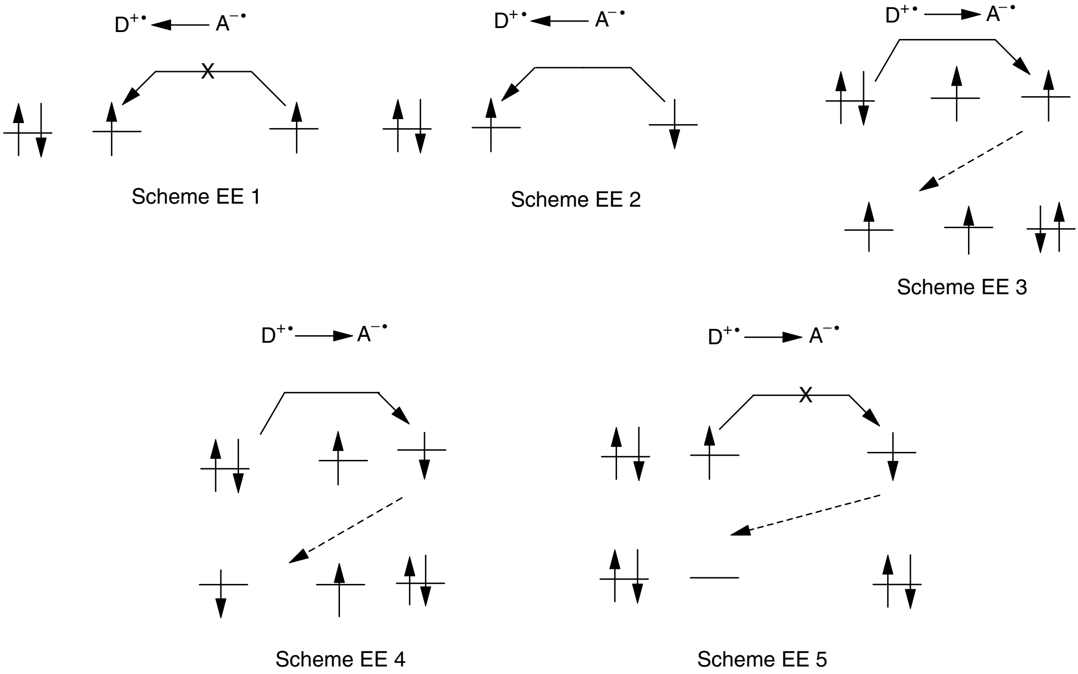
To understand the sample (material) magnetism, one needs to comprehend the nature of molecular magnetism. The two paramagnetic components of the salt can take part in electron exchanges (EE). One type of electron exchange is $D^{+\bullet} \leftarrow A^{-\bullet}$ and the other is $D^{+\bullet} \rightarrow A^{-\bullet}$. These types of electron interactions are depicted in EE graphs from 1 to 5 in Scheme 8.14.

In accordance with the Pauli exclusion principle, electron exchange can take place only between electrons with antiparallel spins. Therefore, from graphs EE1 and EE2, only the EE2 type is permitted. Interactions according to graphs EE3 and EE4 are real, as well. Graph EE3 corresponds to the ferromagnetic orientation of spins. Graph EE5 (one-electron transfer from the cation-radical to the anion-radical) is energetically forbidden.

According to the Hund rule, only the states with maximal spin multiplicity have the lowest energy among all possible states of a given electron configuration. As for multiplicity, it is defined with parallelism in spin orientations. Therefore, the interaction depicted in graph EE3 is the most probable because it, in contrast to that of graphs EE2 and EE4, leads to the state with the maximal spin multiplicity. This is the picture of microscopic ferromagnetism of an ion-radical salt.

In the macroscopic sense, spin-bearing molecules or ions are usually far enough apart. Their spin-coupling energy is small compared with the coupling–breaking thermal energy. Such spins do not couple; instead they form a very weak type of magnet called *paramagnet*. When spins are closer

* In this structure $FeCp_2$ means decamethylferrocene.



SCHEME 8.14

together, the spin-coupling energy increases and may become large enough to enable an effective ferromagnetic or antiferromagnetic coupling.

The ferromagnetic coupling observed for $(FeCp^*_2)^{+\bullet}(TCNE)^{-\bullet}$ leads to a long-range order throughout the solid below a critical temperature (T_C = 4.8 K, where T_C refers to the Curie temperature). Substitution of a bulkier anion-radical component, $(TCNQ)^{-\bullet}$, for the smaller anion-radical component, $(TCNE)^{-\bullet}$, makes magnetic behavior worse. In other words, an increase of the spin density in the smaller acceptor portion of the salt enhances spin coupling and stabilizes the ferromagnetic behavior of the material.

Replacing $(FeCp^*_2)^{+\bullet}$ with nonspin $(CoCp^*_2)^+$ in the salt with $(TCNE)^{-\bullet}$ eliminates magnetic coupling. This demonstrates that both cation and anion of these salts need to have unpaired electrons to stabilize ferromagnetic coupling. In other words, spin sites on both the cation-radical and anion-radical parts of the salt contribute to the material's magnetic properties.

Long-range antiferromagnetic order can, nevertheless, result in the formation of a ferrimagnet below T_C. In the ferrimagnetic state, neighboring electron spins are oriented in opposite directions, but their magnetic moments do not cancel out because the amount of moments oriented in one direction are larger than the amount of moments oriented in the other. Ferrimagnets such as $(Mn^{III}TPP)^+(TCNE)^{-\bullet}$ (TPP is *meso*-tetraphenylporphyrin) has a net magnetic moment. The material is characterized with a T_C of 14 K.

Hence, the ferromagnetic or ferrimagnetic behavior of a material is not a property of a molecule or an ion. Like electric conductivity, it is a cooperative property seen only in the solid state, in assembles of molecules.

Magnets can have behaviors other than ferrimagnetic, ferromagnetic, and antiferromagnetic. For example, *metamagnetism* is the transformation from an antiferromagnetic state to a ferromagnetic state by the application of an external field. The $(MnCp^*_2)^{+\bullet}(TCNQ)^{-\bullet}$ salt, mentioned previously, is an example of metamagnetics. Its transformation into a ferromagnet occurs at 127.36 A · cm^{-1} (1600 oersted) and at a T_C below 2.55 K.

A canted or weak ferromagnet can be formed if spins, which couple ferromagnetically, are only partially aligned. When Buckmingsterfullerene C_{60} reacts with tetrakis (dimethylaminoethylene), $(Me_2N)_2C{=}C(NMe_2)_2$, the salt of C_{60} anion-radical and $(Me_2N)_2C{=}C(NMe_2)_2$ cation-radical is formed to produce a semiconducting material with magnetic ordering at 16 K. However, this material does not have all properties expected for a ferromagnet. This suggests that the material may be either a canted ferromagnet or a spin glass, in which nearby spins align but their direction shifts in different parts of the material. Salts resulted from interactions between tetrakis(dimethylamino) ethylene and larger fullerenes (those with 70, 84, 90, or 96 carbon atoms) do not exhibit magnetic ordering (Wudl and Thompson 1992, Khan 1993, Miller and Epstein 1995).

It would be interesting to test the magnetic properties of C_{60}-based materials cocrystallized with donors. Pure C_{60} crystallizes as a cubic close-packed arrangement of spheres in a face-centered cubic lattice that contains large voids. However, the molecules can be packed more efficiently (particularly in a 1-D manner) by using a co-crystallization agent. For example, it is possible to arrange a supramolecular assembly of C_{60} molecules with *p*-bromocalix[4]arene propyl ether. In such an assembly there are closely packed columns, which are perfectly ordered in a linear fashion (Barbour et al. 1998). The 1-D strands of the fullerene molecules are separated from each other by the calixarene molecules. The calixarenes bearing strong donor fragments could, therefore, present some interesting opportunities.

The theoretical design of donor oligomers that gives parallel spins upon electron transfer is reported (Mizouchi et al. 1995). TTF and TSeF were used as the donor units in the corresponding ion-radical salts. Reviews by Enoki and Miyazaki (2004) as well as Turner and Day (2005) consider and explained magnetic properties of these systems from physical background.

Magnetic interaction between the spins has to be more significant than thermal movement of atoms or ions. When the energy of electron exchange (J) becomes positive, a paramagnetic material is turned into a ferromagnetic one. If $J > kT$ (k is the Boltzmann constant), the perfect order occurs in electron orientation. If, in the sense of absolute values, $J < kT$, thermal movement destroys this order and chaos arises. The point of conversion from order to chaos corresponds to some critical temperature that is called the Curie temperature (T_C). The equality $J = kT_c$ meets the boundary condition of order–chaos conversion. Stronger the interaction, higher the temperature of order loss. In metallic iron, for example, the exchange interaction of electrons is positive and so strong that loss of ferromagnetism takes place only at the very high temperature (1043 K or 770°C). Magnets are useful only below their T_C, which for most purposes must be substantially above room temperature.

Miller and Epstein (1995) have developed an organic-based material that retains magnetic properties up to its decomposition temperature of 350 K (75°C). They have made this magnet by reacting TCNE with $V(C_6H_6)_2$ or with $V(CO)_6$. As a result, TCNE gives the anion-radical coordinated to vanadium, the nonmagnetic metal. Each $[TCNE]^{-\bullet}$ binds up to four vanadium atoms. Each vanadium atom, in turn, is surrounded by up to six ligands, usually coordinating with nitrogen atoms from different $[TCNE]^{-\bullet}$ species. The $[TCNE]^{-\bullet}$ moieties in the assembly are most probably planar, but some of them may be twisted. Molecules of the solvent, such as methylene chloride, may also coordinate to the vanadium. The ability of $[TCNE]^{-\bullet}$ to bind more than one vanadium atom results in the formation of a 3-D network. This network can support the strong spin coupling necessary for such a high T_C. Other solvents such as THF or acetonitrile produce materials with lower T_C, typically about 200 K with THF and 140 K with acetonitrile. When the solvent molecules coordinate to the vanadium, they may block $[TCNE]^{-\bullet}$ sites, thereby reducing the number of connections between spin sites and increasing structural disorder. These changes lead to local random differences in the magnetic interactions.

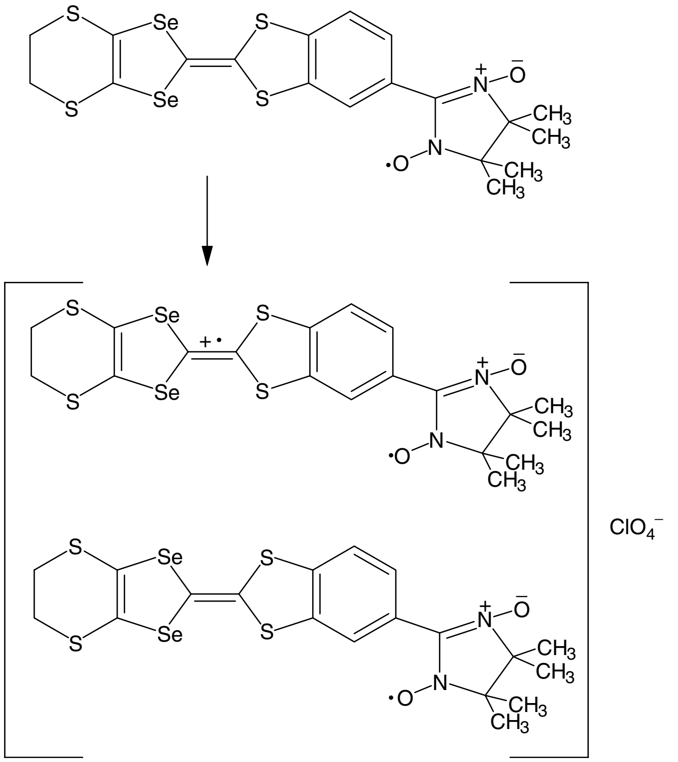
The molecule-based magnet $V(TCNE)(CH_2Cl_2)_y$, sealed in ampoules with an inert gas, can deflect the magnetic field of another magnet. Regrettably, widespread application of this vanadium-TCNE compound will have to wait. It reacts with water readily and explosively with oxygen. Therefore, it is impossible to exploit it in ambient conditions of air and atmospheric moisture.

Ferromagnetic organic materials capable of processing “above room temperature” are technically very attractive. Organic ferromagnetics could be easily deposited upon other materials. Organic magnets can be bent and spread more easily than magnetic (elemental) metals. They might also be cheaper than metal magnets, which are typically produced at vulcanian temperatures. Flexible magnetic coatings and systems for storage of magnetic data are two obvious possible applications. The densities of organic ferromagnetics are lower than those of metals and metal oxides. Moreover, their applications would be possible in medical devices (the magnetic valves in artificial hearts, etc.). Organic magnets could supply magnetic memory. The point is that they possess properties of the so-called spin glasses. Namely, their characteristics can change depending on parameters of the magnetic field they have been in. Among other organic magnetic materials (for instance, based on radicals or carbenes), ion-radicals have a particular advantage. Anion-radicals can be oxidized and cation-radicals can be reduced (reversibly in both cases) into uncharged molecules with no unpaired electrons. In principle, this peculiarity permits molecular magnetism to be switched on or off and turned up or down by application of an external electric potential to control the redox state (and the spin state) of a molecule or, ultimately, of a bulk material.

Coronado et al. (2000) described a hybrid material that opens a new frontier in molecular electronics. They have created an ion-radical salt that can behave simultaneously as a magnet and as an electrical conductor. Crystals of composition $[BEDT\text{-}TTF]_3^{+\bullet}[Mn^{II}Cr^{III}(C_2O_4)_3]^-$ were prepared by electrocrystallization of a methanol/benzonitrile/dichloromethane solution containing chromium oxalate $[Cr_2(C_2O_4)_3]$, Mn(II) ion and a suspension of bis(ethylenedithio)tetrathiafulvalene [BEDT-TTF]. The structure of the material prepared consists of layers of $[BEDT\text{-}TTF]_3^{+\bullet}$ cation-radicals alternating with honeycomb layers of $[Mn^{II}Cr^{III}(C_2O_4)_4]^-$ bimetallic oxalato complex anions. The $[BEDT\text{-}TTF]_3^{+\bullet}$ components are tilted at an angle of 45° with respect to the $[Mn^{II}Cr^{III}(C_2O_4)_3]^-$ inorganic layer. This opens up the possibility for the two components to act independently: The cation-radical plays the role of an organic metal, whereas the bimetallic complex acts as an artificial magnet. The hybrid material becomes a magnet only below 5.5 K, so cooling with liquid helium is necessary. Such materials are now primarily of fundamental interest. Nevertheless, this ion-radical salt gives an attractive example of future materials that can be both ferromagnetic and electrically conductive. This unique feature, which is made possible by the molecular nature of the material, may yield unexpected physical behavior. One could imagine, for example, materials that will really deliver smaller and smaller devices offering more than one function. Usually, ferromagnetism and superconductivity are considered as properties that, like oil and water, do not mix.

The synthesis, structure, and electric and magnetic characteristics were recently described for two other salts formed with BEDT-TTF and hexacyanoferrate, $(Et_4N^+)_3[Fe(CN)_6]^{3-}$ or nitoprusside and $K^+_2[Fe(CN)_5NO]^{2-}$. The study sheds light on the general peculiarities of making two-network solids by combining magnetic anions, which provide localized magnetic moments, with partially oxidized organic donor molecules, which support electronic conduction (Clemente-Leon et al. 2001). The two salts mentioned, present very different stoichiometry: $[(BEDT\text{-}TTF)_4(NEt)_2][Fe(CN)_6]$ and $[(BEDT\text{-}TTF)_2]$ $[Fe(CN)_5NO]$. They also present different packing motifs, and the oxidation states of the BEDT-TTF moiety. For the first salt, the molecular arrangement in the organic layer is centrosymmetrical-eclipsed dimers. The organic network has a 2-D character: Each dimer of a given layer is orthogonal to the closest dimer situated on the next layer. Each BEDT-TTF moiety bears one-fourth of the unit positive charge, whereas the whole BEDT-TTF ensemble exists in a mixed valence state. That gives rise to a high room-temperature electric conductivity and a temperature-independent paramagnetism. The inorganic anion also contributes to the paramagnetism.

The second salt presents a structure where the anions occupy the tunnels formed by BEDT-TTF dimers. BEDT-TTF bears the unit positive charge. This salt behaves like a semiconductor with a very low room-temperature electric conductivity. The unpaired electrons on the organic cation-radicals are strongly antiferromagnetic coupled, giving rise to a diamagnetic behavior of the second salt, because the nitroprusside anion is also diamagnetic.



SCHEME 8.15

Matsushita et al. (2007) synthesized a genuine organic paramagnetic conductor. Electrocrystallization of the thia-selena compound bearing an *N*-oxyl leads to a perchlorate triple salt, which displays as magnetism as electric conductivity (see Scheme 8.15).

Scheme 8.15 compels attention to the following features of the resulting species: Complexation of the cation-radical with parent neutral counterparts enhances mobility of an unpaired electron. Introduction of selenium (heavier and bulkier atom) increases the overlap among donor planes due to the better chalcogen–chalcogen intermolecular contacts. The presence of the paramagnetic nitroxyl moiety is decisive for magnetism of the product.

The results presented support the view that magnetism and superconductivity in ion-radical salts have a common electronic origin (Wilhelm et al. 2001). By and large, molecular magnetism is a fresh research area, and it has grown rapidly in the past two decades (see a review by Miller 2000). Among industrial corporations elaborating organic magnets, the largest and the most powerful are American DuPont and IBM. Data from existing publications are still not numerous. However, it is obvious that this is a promising field and that modern scientists have declared the basic ideas on ferromagnetism of organic ion-radical salts correctly.

8.6 LUBRICATION IN TERMS OF ION-RADICAL ORGANIC CHEMISTRY

Mechanical processing (e.g., abrasion) of metallic surfaces causes the emission of electrons; this is known as the Kramer effect (Kramer 1950). The effect has been shown by the measurement of self-generated voltages between two metallic surfaces under boundary lubrication (Anderson et al. 1969, Adams and Foley 1975). The exoelectrons have a kinetic energy from 1 to 4 eV (Kobzev 1962) and they may initiate some chemical reactions. For instance, if the metal (whose surface has been *worked*) is placed in an aqueous solution of acrylonitrile, the latter forms an abundant amount of an insoluble

polymer, and the polymer formed accumulates after 4 days of the contact. The same solution of acrylonitrile contains no polymer even after 4 months of contact with a piece of *nonworked* metal. The following sequence of the reaction steps was proposed to explain the formation of polymer (Ferroni 1955):

$$H_2O + e \rightarrow H^\bullet + OH^-;\ H^\bullet + O_2 \rightarrow HO_2^\bullet;\ HO_2^\bullet + H_2O \rightarrow H_2O_2 + {}^\bullet OH$$

$$CH_2{=}CHCN + {}^\bullet OH \rightarrow HOCH_2CH^\bullet CN$$

$$HOCH_2CH^\bullet CN + CH_2{=}CHCN \rightarrow HOCH_2CH(CN)CH_2CH^\bullet CN, \text{ etc.}$$

Boundary lubrication is defined by the properties of the surfaces and the lubricants—the properties other than viscosity. Surface friction generates the emission of electrons, photons, ions, neutral particles, gases (e.g., oxygen), and x-rays. According to the theme of this book, reaction of organic lubricating materials with triboemitted electrons will be considered in Section 8.6.

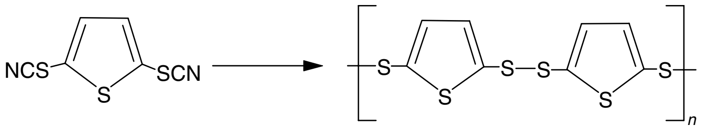
Electron emission occurs when plastic deformation, abrasion, or fatigue cracking disturbs a material surface. Triboelectrons are emitted from freshly formed surface. The emission reaches a maximum immediately after mechanical initiation. When mechanical initiation is stopped, the emission decays with time. Strong emission has been observed for both metals and metal oxides. There is a strong evidence that the existence of oxides is necessary. The exoelectron emission occurs from a clean, stain-free metallic surface upon adsorption of oxygen (Ferrante 1977).

Goldblatt (1971) explained the lubricating properties of polynuclear aromatics by assuming that anion-radicals are generated at the freshly abraded surface. Low-energy electron emission (exoemission) creates positively charged spots on a surface, generally on top of surface asperity. At the same time, the exoemission produces negatively charged anion-radicals of lubricant components. The positively charged metallic surface attracts these negatively charged species.

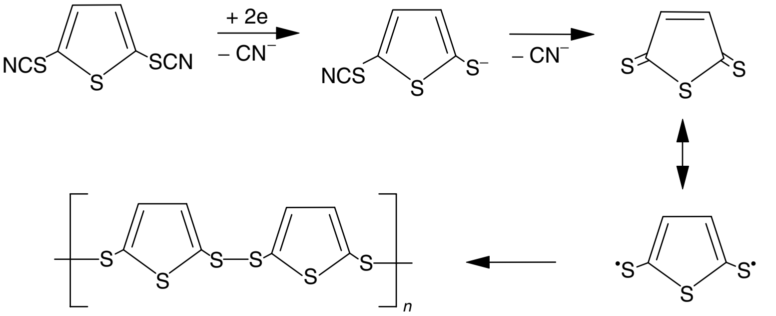
The anion-radicals formed are involved in further reactions that result in formation of polymers and organometallics. Whereas the reactions within organic additive mixtures lead to polymeric films, organometallic compounds are understandable as products of interaction between the metallic surface and the radicals. Both polymeric films and organometallic species can protect the rubbing surface from wear. Sometimes, introduction of ready-made metal complexes with organic ligands into lubricating compositions, brings a positive effect (Sulek and Bocho-Janiszewska 2003, Chigarenko et al. 2004). Destruction of these complexes originates the polymeric film and leads to liberation of the metal from the complex. The metal is doped into the mating metal surface. This process results in metallurgical changes on the metal surface, making it harder than the steel core of the lubricated device. Importantly, the protective layer formed is continuously renewed.

Many known structural features of lubricant activity become understandable in the framework of the ion-radical conception. Thus, it is generally accepted that the extreme pressure performance of disulfides (R–S–S–R) is better than that of monosulfides (thioethers, R–S–R), see Forbes' review of 1970. The difference was simply explained with the ion-radical conception. Monosulfides are reduced less readily than disulfides. Because of the nature of the antibonding orbital hosting the unpaired electron, the sulfur–sulfur bond is elongated markedly in R–S–S–R. Dissociation energy of this elongated bond becomes much smaller than that in the neutral molecule regardless of the aryl or alkyl character of bound substituents (Antonello et al. 2002). Reductive cleavage of disulfides with generation of active species RS^- and $RS^\bullet$ proceeds readily. Accordingly, disulfides exhibit more efficient load-carrying properties than monosulfides.

Dithiyl radicals seem to be especially attractive because they can form extended homopolymer films. If one uses a simple compound that is capable of forming dithiyl radical, then that can open a way for formulation of a lubrication composition. For example, a poly(disulfide) was obtained as a result of a two-electron transfer to 2,5-di(thiocyanato)thiophene (Scheme 8.16) (Todres et al. 1979, Todres 1991).



SCHEME 8.16



SCHEME 8.17

This linear polysulfide obviously formed according to the sequence 2,5-di(thiocyano) thiophene → potassium 2-mercaptido-5-thiacyanonothiophene → (tristhio)maleic anhydride ↔ thiophene-2,5-disulfenyl biradical (the diradical valence tautomer) → the depicted linear polymer in which the thiophene rings are connected through disulfide bridges (Scheme 8.17).

The reaction of Scheme 8.17 provides a good reason to probe such very simple compounds as sources of lubricating films for rubbing metallic surfaces.

The work function of the rubbing surfaces and the electron affinity of additives are interconnected on the molecular level. This mechanism has been discussed in terms of tribopolymerization models as a general approach to boundary lubrication (Kajdas 1994, 2001). To evaluate the validity of the anion-radical mechanism, two metal systems were investigated, a hard steel ball on a softer steel plate and a hard ball on an aluminum plate. Both metal plates emit electrons under friction, but aluminum produced more exoelectrons than steel. With aluminum, the addition of 1% styrene to the hexadecane lubricating fluid reduced the wear volume of the plate by over 65%. This effect considerably predominates that of steel on steel. Friction initiates polymerization of styrene, and this polymer formation was proven. It was also found that lauryl methacrylate, diallyl phthalate, and vinyl acetate reduced wear in an aluminum pin-on-disc test by 60–80% (Kajdas 1994).

Triboemission also explains steel lubrication by perfluoropolyalkyl ethers (PFPAEs). PFPAEs possess remarkable properties that make them the lubricant of choice in demanding applications such as magnetic recording media, the aerospace industry, satellite instruments, and high-temperature turbine engines. The physical properties of PFPAEs that enable them to perform lubricating functions in severe environments are their nonflammability, excellent viscosity index, low pour point, and low volatility. Chemically, the most unique property of PFPAEs is their stability up to 370°C in an oxidizing environment (Helmick and Jones 1994). Though PFPAEs have excellent thermal stability in a metal-free environment, this stability is significantly decreased to about 180°C when metal alloys and metal oxide surface are present (Koka and Armatis 1997). This poses a major problem in the practical utility of these lubricants since metals and metal oxides are prevalent in tribological operations.

Let us consider the tribological behavior of one major commercial product of the PFPAE series. This product bears the trade name of PFAE-D; its structure is $CF_3(OCF_2)_x(OCF_2CF_2)_y(OCF_2CF_2CF_2)_z$ OCF_3. The molecule contains OCF_2O units that have been attributed to the lower thermal stability of the material compared with other commercial fluids. To gain insight into the decomposition mechanism of the polymer, Matsunuma et al. (1996) selected a compound containing five (CF_2O)

units as a model for the commercially equivalent fluid. The authors performed a semiempirical molecular orbital calculation comparing optimized molecular structures with the energies of bond breaking. In comparison to the neutral molecule, the formation heat in the corresponding anion-radical was markedly lower. Electron attachment to the neutral species loosened the C–O bond. Cleavage of the weakest C–O bond of the anion-radical produced the anion and the neutral-radical:

$$CF_3{-}OCF_2{-}OCF_2{-}OCF_2{-}OCF_2{-}OCF_2{-}CF_3 + e \rightarrow [CF_3{-}OCF_2{-}$$

$$OCF_2{-}OCF_2{-}OCF_2{-}OCF_2{-}OCF_3]^{-\bullet} \rightarrow$$

$$\rightarrow CF_3{-}OCF_2{-}OCF_2{-}OCF_2{-}O^- + {}^\bullet CF_2{-}OCF_2{-}OCF_3$$

The shortened anion has a weak $CF_2{-}OCF_2$ bond. The degradation of this anion proceeds in a stepwise manner:

$$CF_3{-}OCF_2{-}OCF_2{-}OCF_2{-}O^- \rightarrow CF_3{-}OCF_2{-}OCF_2{-}O^- + CF_2{=}O\uparrow$$

$$CF_3{-}OCF_2{-}OCF_2{-}O^- \rightarrow CF_3{-}OCF_2{-}O^- + CF_2{=}O\uparrow$$

$$CF_3{-}OCF_2{-}O^- \rightarrow CF_3{-}O^- + CF_2{=}O\uparrow$$

Favorable factors for this successive degradation are the low-estimated activation energy and the liberation of the volatile carbonyl fluoride product at room temperature. Strom et al. (1993) observed degradation of PFPAEs during friction tests on magnetic disks using a mass spectrometer. The successive degradation of PFPAEs, which produces carbonyl fluoride, was monitored. This process was called an "unzipping mechanism" (Kasai 1992, Strom et al. 1993).

Zinc dialkyl/diaryl dithiophosphates are widely used as antiwear additives in engine oils to protect heavily loaded engine parts from excessive wear. They are also used as antiwear agents in hydraulic fluids. The salts are effective oxidation and corrosion inhibitors, they also act as detergents. During friction, these salts form anion-radicals that are successfully cleaved (Kajdas et al. 1986).

$$(RO)_2P(S)S{-}Zn{-}SP(S)(RO)_2 + e \rightarrow (RO)_2P(S)S^- + [ZnSP(S)S(RO)_2]^\bullet$$

Polymers originating from $[ZnSP(S)(RO)_2]^\bullet$ radical form lamellar aggregates, which contain Zn, P, S, O, and C, but not Fe (Berndt and Jungmann 1983, Sheasby and Rafael 1993). These aggregates transform into zinc sulfide and nonmetallic polymers at high temperatures. Probably, some intimate interaction between the lubricant and the steel surface precedes generation of the radicals. Under the conditions of electron transfer, thione-thiol rearrangement of the type P(S)OR → P(O)SR takes place (Kajdas et al. 1986). The rearrangement changes the bond polarizability of metal dialkyldithioposphates and enhances the driving forces of all chemical processes described.

Triboemission takes place at the asperities of a freshly abraded metallic surface. The surface spots gain a positive charge as a result of triboemission. In other words, fresh surfaces prepared by machining metals are chemically hyperactive for a short period. As shown (Smith and Fort 1958), such surfaces adsorb nonadecanoic acid from cyclohexane solution to a monolayer. Realization of this coverage is a consequence of a chemical reaction between the fatty acid and the atoms of the fresh metal surface; this is activated by emission of exoelectrons from the surface. This chemical reaction produces a metal soap. Adsorption is a function of the activity of the metal, degree of activation of the machined surface, lifetime of the activated state, and the free-energy requirements of the soap-forming reaction. The adsorbed films are not static. Soap molecules are continually desorbed. The vacancies thus created in the adsorbed layer are filled by diffusion of additional fatty acid to the surface, and then the reaction proceeds *in situ* to form additional molecules of the

adsorbed metal soap. The rates of this desorption and adsorbed-film replenishment decrease with the age of the metal surface. Kinetics of both these processes and of the initial chemisorption are a function of the surface activation.

Naturally when such renewable films acquire a polymeric structure, their lubricating activity is enhanced. Thus, the wear test of a four-ball machine showed that dihydroxydocosanoic acid had a good antiwear property approaching that of zinc dialkyldithiophosphate, the traditional antiwear agent. The order of antiwear properties for the C_{22} acids was 13,14-dihydroxydocosanoic acid >13- or 14-monohydroxydocosanoic acid > docosanoic acid (no hydroxy substituent). One can see that the antiwear properties of base stock are improved by introducing the hydroxyl group into docosanoic acid. It was revealed by Auger electron or infrared spectroscopy that dihydroxy docosanoic acid forms an oxygen-enriching protective film. Namely, this acid produces the netlike polyester at the expense of the reaction between the carboxyl and hydroxy groups (Hu 2002). It is the tribochemical reaction within the boundary lubrication that is the basis for the improved antiwear activity of dihydroxydocosanoic acids.

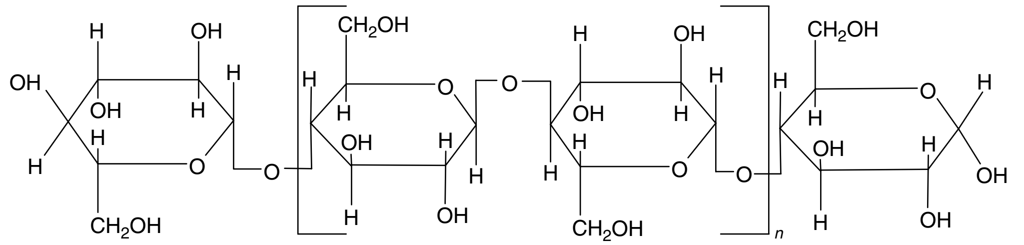
Interestingly, 5-allyl-2-methoxyphenol is not polymerized during friction, but undergoes transformation into 2-methoxyphenol-5-(methylcarboxylate) under the action of triboemission (Molenda et al. 2003). Seemingly, the carboxylate then forms chelate compounds with the steel surface iron.

Note that, to understand the chemical behavior of lubricant components during boundary lubrication, the concept of triboemission should be put forward. The concept is based on the ionization mechanism of lubricants caused by the action of low-energy electrons (1–4 eV). The electrons (exoelectrons) are spontaneously emitted from the fresh surfaces that are formed during friction. The principal thesis of the model is that lubricant components form anion-radicals, which are then chemisorbed on the positively charged areas of rubbing surfaces. The model encompasses the following major stages: (1) the low-energy process of electron emission and the creation of positively charged spots; (2) the interaction of emitted electrons with lubricant components and the generation of anion-radicals, anions, and radicals; (3) the reactions of these anion-radicals and anions with positively charged metal surfaces, forming films to protect the surface from wear; and (4) the cracking of chemical bonds to produce other radicals. The model explains many lubrication phenomena in which antiwear and extreme pressure additives are involved. It spurs the design of new additives and lubricating compositions. For the interested readers, a review “Importance of the Triboemission Process for Tribochemical Reaction” by Kajdas (2005) is recommended.

8.7 ION-RADICAL ORGANIC CHEMISTRY IN ITS CONTRIBUTIONS TO WOOD DELIGNIFICATION AND FOSSIL-FUEL DESULFURIZATION

8.7.1 Paper Fabrication

Paper products (newsprint, tissue, packaging, etc.) are made from pulps that consist of natural fibers derived from vascular plants such as trees, sugar cane, bamboo, and grass. The vascular fiber walls are composed of bundles of cellulose polymeric filaments. This long, linear glucose polymer is what paper is made from. The polymer has the structure shown in Scheme 8.18.



SCHEME 8.18

Nature rigorously shields the glucose polymer from harm by enclosing it in a mixture of barrier polymers. In wood, cellulose fibers are protected in a matrix of lignin. (The term "lignin" is derived from the Latin word "lignum," meaning wood.) Plants synthesize lignin, mainly to provide strength and protection. In the sense of protection, lignin is just the wrapping material that protects cellulose from fungal damage. What the fungus really wants is the cellulose, which has an ordered structure and gives them the same piece each time the fungus degrades it. Lignin is an amorphous, 3-D, and water-insoluble polymer. It is stereo-irregular, and there are no large pores in it. Lignin is formed by a peroxydase-catalyzed polymerization of the methoxy-substituted 4-hydroxycinnamyl alcohols. Scheme 8.19 depicts these alcohols, from left to right: 4-hydroxy-cynnamyl- (or *p*-coumaryl-) alcohol, 4-hydroxy-3-methoxy-cynnamyl- (or coniferyl-) alcohol, and 4-hydroxy-3,5-dimethoxy-cynnamyl- (or sinapyl-) alcohol.

The initially formed phenoxy radicals randomly combine to form a variety of bonds. Scheme 8.20 shows major linkages between units in softwood lignin. Hardwood lignins are similar, but contain varying quantities of the 3,5-dimethoxylated aromatic rings.

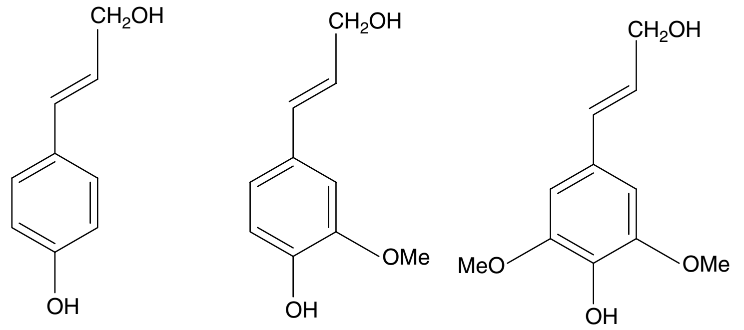
In lignin, there are attendant ketone (sometimes, quinone) chromophoric moieties that give it a yellow/brown color. Cellulose is a white substance, which provides the desired strength and brightness properties to the paper products. The strength and whiteness of a paper product depends on the extent of removal of lignin from the pulp fibers. Row woods contain as much as 20–30% lignin.

Various modifications have been made to the conventional chemical pulping process to increase the extent and selectivity of delignification. Delignification occurs through the fragmentation of the lignin polymer, followed by the ionization and solubilization of the molecular fragments. This degradation process is characterized by cleavage of the aryl-propane side chains, ether-bond cleavage, aromatic ring opening, hydroxylation and the formation of carboxylic acids. With the possible exception of the carboxylic acid–producing reaction, most of the reactions have been adequately rationalized by the formation of ion-radicals (Schoemaker 1990, Schoemaker and Piontek 1996, Have ten and Teunissen 2001). The following schemes present some examples.

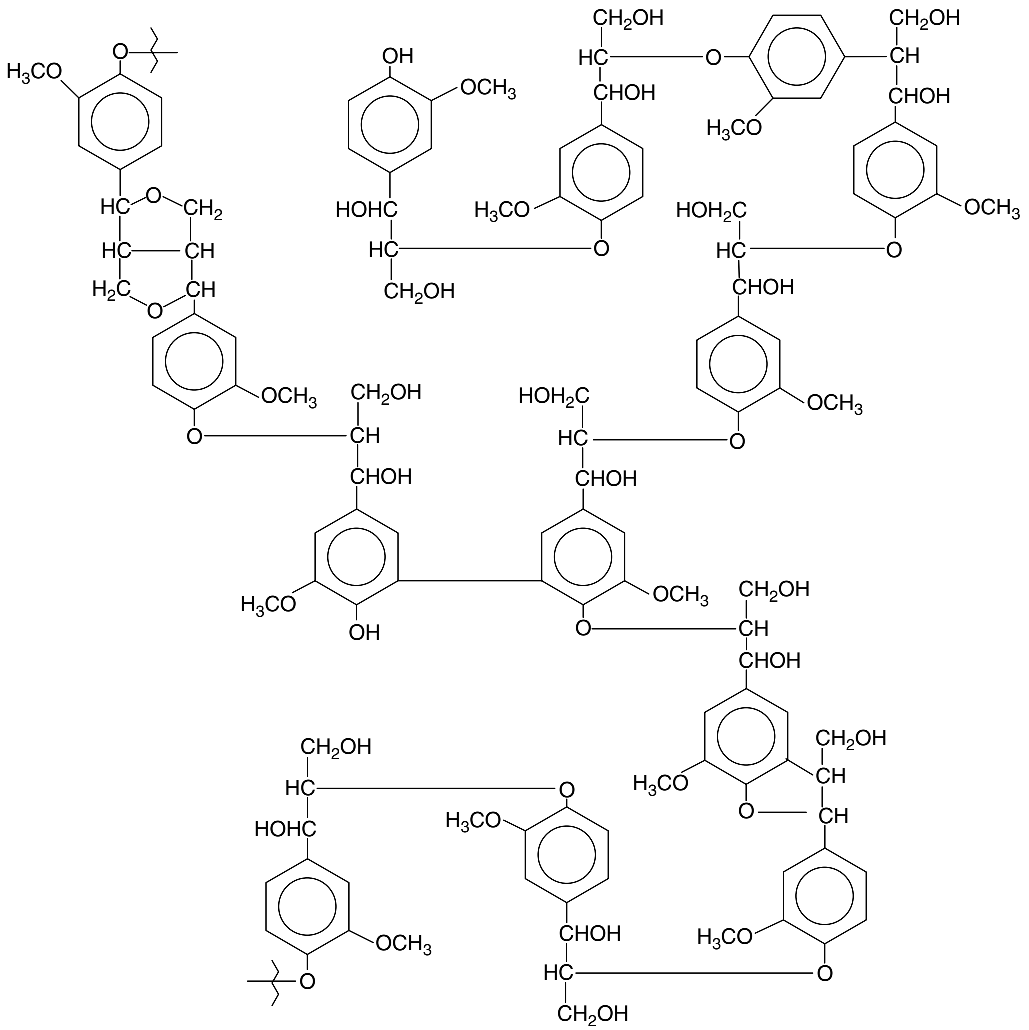
As for demethoxylation, it is known that 1,4-dimethoxybenzene is oxidized to the corresponding benzoquinone. The reaction takes place under conditions of bio-oxidation and proceeds through intermediacy of an ESR-detectable cation-radical (Kersten et al. 1985) (Scheme 8.21).

As for β-*O*-4 ethereal bond cleavage, reaction of the primary cation-radical with solvent water under the same conditions of bio-oxidation was shown to form an arylglycerol and the corresponding phenoxy radical (Kirk et al. 1986, Fabbri et al. 2005) (Scheme 8.22). Since the β-*O*-4 ethereal bond is the most abundant type of interunit linkage in the lignin polymer, this ethereal bond cleavage represents an important depolymerization reaction.

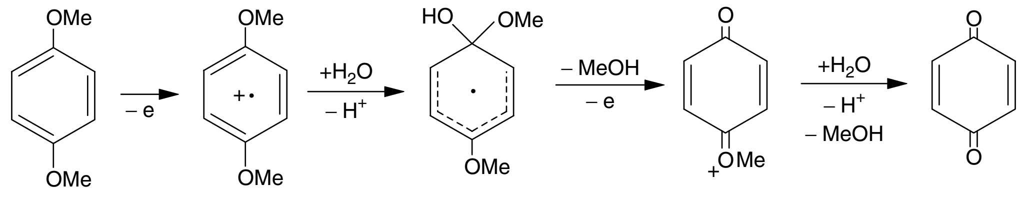
To prepare paper, felled timber is transformed into pulp. The ready-made paper, however, contains some residual lignin and undergoes slow yellowing caused by the sunlight. The coloration results from the formation of quinones. This role of quinones has already been mentioned.



SCHEME 8.19

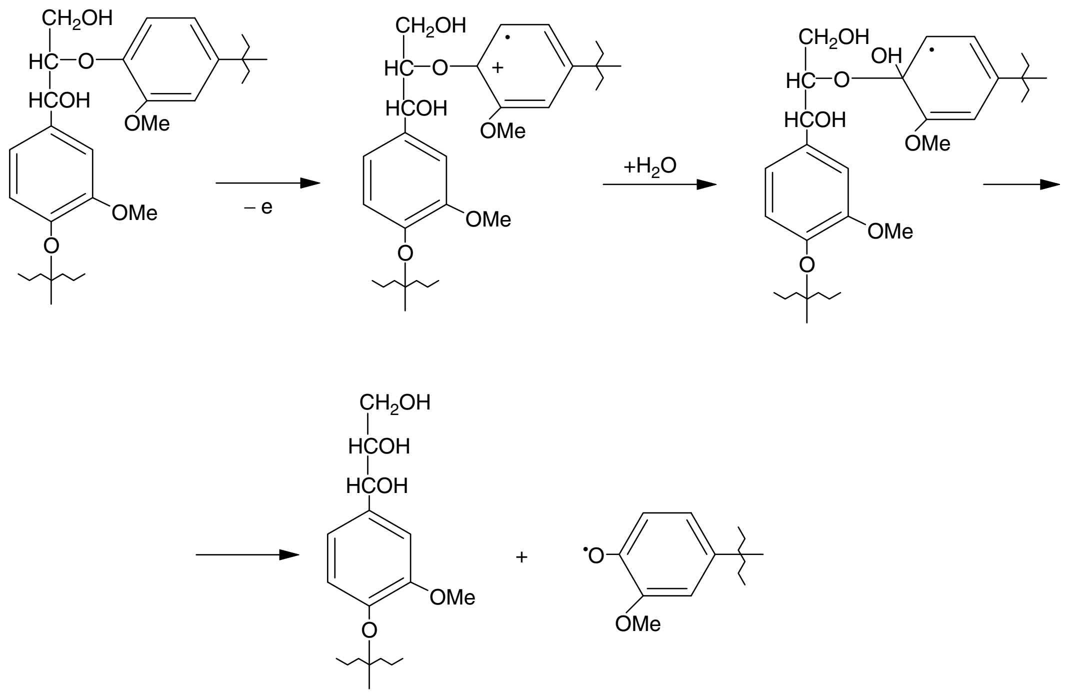


SCHEME 8.20



SCHEME 8.21

Durbeej and Eriksson (2005) obtained more accurate information that the paper-yellowing quinones originate from diguaiacylstilbenes. These stilbenes are generated during the mechanical grinding, disc refining, and alkaline peroxide treatment of pulps. The precursors of stilbenes, in turn, are diarylpropane units of lignin. Photoirradiation generates cation-radicals that disintegrate producing phenoxy-type radicals and further form the corresponding quinones with adsorption characteristics yielding a yellow coloration. Recently, some modifications were proposed for the paper fabrication.



SCHEME 8.22

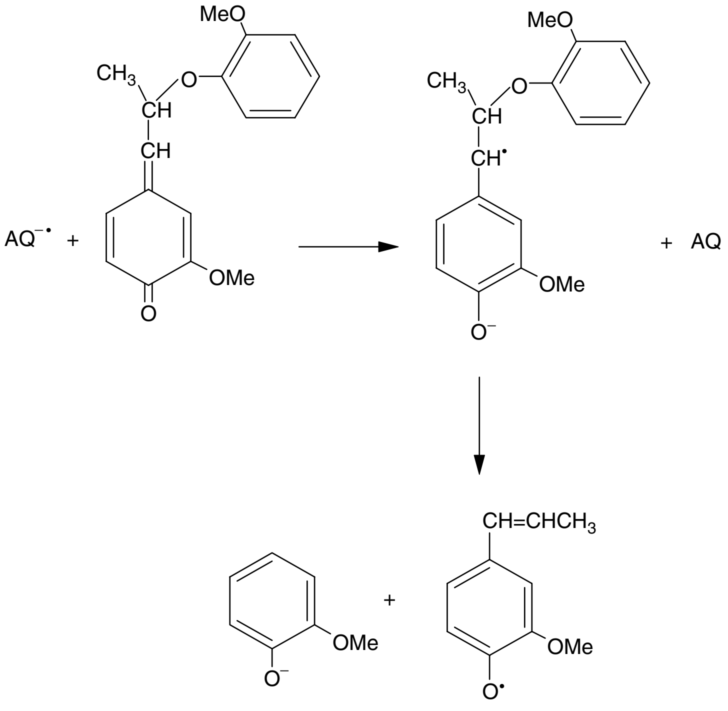
One modification that pertains to the present book is the role of anthraquinone (AQ) in the pulping process. Under conditions of alkaline pulping, carbohydrates in the wood reduce AQ into an anion-radical ($AQ^{-\bullet}$). Experiments with lignin quinonemethide as a model compound showed that the AQ anion-radical caused fragmentation of the quinonemethide (Scheme 8.23).

The reaction of the Scheme 8.23 results in the formation of a substituted phenolate ion and a radical. The radical is further reduced by the next $AQ^{-\bullet}$ (Dimmel et al. 1985). The keto groups in lignin can be involved in the analogous reaction with $AQ^{-\bullet}$. This leads to formation of the ketyl functions which originate analogous fragmentation processes.

Several pulp mills now use AQ on a commercial basis (Oloman 1996). According to Oloman, the addition of AQ to pulping liquor in an amount of 1 kg AQ per ton of pulp increases the pulp yield from starting woods by about 1%. This complementary action gives rise to increased revenue of about $2 million per year for a pulp mill with a daily productivity of 1000 t.

The pulp industry also uses another anion-radical precursor, namely 1,4,4a,9a-tetrahydro-anthraquinone. The product is easily obtained from cheap starting materials—1,4-naphthoquinone and butadiene—in the Diels–Alder reaction. The mixture of tetrahydroanthraquinone with sulfite is very effective. The main role of sulfite in delignification during alkaline sulfite-quinone pulping is to decrease the condensation reactions of lignin. Sulfite does not play an important role in cleaving the β-*O*-4 ethereal bonds of lignin (Ohi et al. 1994).

At present, attention is paid to microorganisms that can oxidize organic compounds and act, after that, as electron sources (see reviews by Van Aken and Agathos 2001 alongside by Lovely 2006). In particular, fungi were discovered with a special ability to digest lignin in a variety of woods (Srebotnik et al. 1994, 1997). The discovery opened a simple and time-controlled biopulping process: Wood chips are steamed to eliminate the native microorganisms, and then cooled and inoculated with a suspension of the fungus *Ceriporiopsis subvermispora* in mixture of water and corn steep liquor. The liquor, a by-product of the starch industry, furnishes a growth medium for the fungus. Only 0.25 g of fungus is needed to treat 1 t of wood chips.



SCHEME 8.23

The bacterial cleavage of lignin develops through one-electron oxidation mechanism. The fungus breaks the bond between the side chain α- and β-carbons as well as the bond between the side chain β-carbon and the aryl oxygen. The unidentified one-electron oxidant generates cation-radical subunits in lignin. Undoubtedly, the fungus produces this oxidant (Hammel et al. 1985, Kersten et al. 1985).

The ensuing reactions of the cation-radicals include $C_\alpha - C_\beta$ cleavage, demethoxylation and other ethereal bond cleaving reactions, hydroxylation of benzylic methylene groups, oxidation of benzylic alcohols, decarboxylation, the formation of phenols and quinones, and the aromatic ring cleavage. In these processes, reaction of oxygen with intermediate radicals occurs, resulting either in oxygen incorporation or in oxygen activation (i.e., reduction to the superoxide ion, see Section 1.7). Incorporation of oxygen from the ambient water is also possible (in the presence of an oxidant).

During 2-week biopulping process, the linkages that connect lignin subunits are being cleaved hence making the wood soft. Biopulping is stopped well before the fungus can attack cellulose, which takes place no sooner than 6 weeks after inoculation. Paper produced from biopulped chips is stronger than paper derived from conventional pulp. Mills that produce paper for magazine printing can save $13 per ton of pulp and retain paper quality by shifting to biopulping. Fungal pretreatment of wood chips can cut the energy cost of conventional pulping by 30%, a savings of $10 per ton of pulp produced. Certainly, holding wood pulp for 2 weeks in a reactor is unacceptable for mills that are producing 1000 t of pulp per day. Hence, systems are needed that would be stable at high temperatures and oxidize lignin in 1 or 2 h. The use of hyperthermophilic bacteria and some of their cloned modifications is promising (Brennan 1998).

Till now, *C. subvermispora* and *Phanerochaete chrysosporium*, the white-rot fungi, remain the best degraders of lignin. They owe their "white-rot" name to the specific bleaching process that occurs during the fungal degradation of wood. It should be important to repeat that the lignin-degradation function of the fungi is aimed to prepare the access to more metabolizable

cellulose containing in woods under the lignin protection. The white-rot fungi excrete lignin peroxidase (LigP). In particular, the enzyme was isolated from lignolytic cultures of *P. chrysosporium* (Tien and Kirk 1983, Glenn et al. 1983). LigP is a glycoprotein containing an iron(III)-protoporphyrin IX with a histidine residue coordinated to the iron atom. Under natural conditions, hydrogen peroxide reacts with LigP, hereinafter denoted as Por-Fe(III), and generates oxyferryl heme porphyrin π cation-radical, $Por^{+\bullet}$–Fe(IV)=O. Further reaction of $Por^{+\bullet}$–Fe(IV)=O complete the catalytic cycle:

$$Por^{+\bullet}\text{–Fe(IV)=O} + \text{Ar–CH(OH)–CH(R)O–Ph} \rightarrow \text{Por–Fe(IV)=O} + Ar^{+\bullet}\text{–CH(OH)}$$

$$\text{–CH(R)O–Ph; } Ar^{+\bullet}\text{–CH(OH)–CH(R)O–Ph} \rightarrow Ar^{\bullet}\text{–}C^{\bullet}\text{(OH)–CH(R)O–Ph} + H^{+\bullet};$$

$$Por^{+\bullet}\text{–Fe(IV)=O} + \text{Ar–CH(OH)–CH(R)O–Ph} + H^{+} \rightarrow$$

$$\text{Por–Fe(III)} + H_2O + Ar^{+\bullet}\text{–CH(OH)–CH(R)O–Ph}$$

As to $Ar^{\bullet}$–$C^{\bullet}$(OH)–CH(R)O–Ph, this radical undergoes oxidative degradation according to reactions described above for the lignin fragmentation (Baciocchi et al. 2003). To say briefly, bacterial lignin splitting principally follows the same way that has been shown for the chemical one-electron oxidation in the beginning of this section.

This section cannot be finished without noting that there is one unsolved (and important) problem concerning a small amount of residual lignin in the ready-made paper. An anion-radical mechanism has been proposed as one of the chemical reactions contributing to the photoinduced degradation of residual lignin leading to photoyellowing of paper (Andersen and Wayner 1999). Such a process leads to the ketyl anion-radical formation. (Ketones of complex structures are also present in lignin.) The ketyl anion-radicals give rise to phenoxides as a result of their fragmentation. Oxidation transforms the phenoxides into phenoxyl radicals and, ultimately, into quinones. The latter are the species responsible for the yellow color. Andersen and Wayner (1999) concluded "It is likely that the strategies to prevent or inhibit photoyellowing of paper will have to be reevaluated to take these mechanistic possibilities into account." This problem remains perplexing and deserves further experimental and theoretical studies.

8.7.2 Manufacture of Commercial Products from Delignification Wastes

The alkaline oxidative cleavage of quaicol or lignosulfonates (sulfite-spent liquor from cellulose production) is another important reaction of wood chemistry. Such typical one-electron oxidants as nitroarenes and transition metal salts are used, sometimes with participation of oxygen. The waste products of the cellulose manufacturing are sources to obtain very cheap vanillin and veratric acid. In its turn, this is profitable for production of mebeverine, vesnarinone, and itopride, the medications that are antispasmodic cardiotonic and gastric prokinetics agents. The alkaline oxidative-cleavage reaction includes a cation-radical step and proceeds through the cleavage of the side chain bonds. The cleavage is made possible by the significant weakening of the C_α–C_β bond induced by the formation of cation-radical fragments.

During this oxidation process, the lignin biopolymer is degraded into low-molecular-weight phenolic compounds that also contain cabonyl groups: ketones, aldehydes, and carboxylic acids (Freudenberg et al. 1940, Fisher et al. 1988). Leopold (1950, 1952) has reported that guaiacol derivatives were oxidized to give high yields of vanillin under rather drastic conditions of alkaline nitrobenzene oxidation. The method requires a reaction temperature of 170–190°C, a pressure of 10–12 atm, and a pH of 13–14. However, by introduction of the more powerful oxidant, 1,3-dinitrobenzene, the oxidation process proceeds smoothly at atmospheric pressure and the much lower reaction temperature of 100°C (Bjorsvik et al. 2001, 2002). According to the authors, the dinitrobenzene

anion-radicals are the driving species of the reaction. Thus, the transformation of mandelic acid (the urinary antiseptic) into benzoic acid proceeds through the following mechanism (all the one-electron oxidation steps include transformation of dinitrobenzene into its anion-radical):

$$PhCH(OH)COOH \rightarrow PhCH(O^-)COO^- \rightarrow PhCH(O^\bullet)COO^- \rightarrow HCOO^- + PhCH^{(\bullet)}{=}O;$$

$$PhCH^{(\bullet)}{=}O \rightarrow PhC^{(+)}{=}O;\ PhC^{(+)}{=}O + {}^-OH \rightarrow PhCOOH$$

The chemical and enzymatic oxidative degradation of lignin (and coal) is used to obtain not only vanillin and benzoic acid, but also other aromatics (Baciocchi et al. 1999, references therein). In principle, lignin could be a major nonfossil and renewable source of aromatic compounds, a feedstock for synthesis of useful products. The problem deserves finding new ion-radical routes to cleave lignin. At present, there is some shortage in oil, gas, and even coal, which had usually been well-available natural sources of aromatics. In the near future, biomass may (and must) replace fossil-originated materials in the manufacture of commercial carbon-based products.

8.7.3 Desulfurization of Fossil Fuels

In various fossil fuel conversion processes, especially in combustion, sulfur-containing components are released into the atmosphere. This pollution proceeds predominantly in the form of sulfurous anhydride, which is toxic and causes acid rains. For coal, the presence of sulfur in coke beyond a certain limit makes it unsuitable for metallurgical purposes. Deleterious effects observed also include corrosion of boilers, underground pipelines, and metallic equipment. There are a lot of inorganic and organic impurities in oils and coals that contain sulfur. Processes of separation of inorganic sulfur-containing impurities are well developed. As to organic desulfurization, various physical, microbial, and chemical methods are known. The microbial and physical methods are still ineffective. Chemical methods of desulfurization are resultative and their further improvement is actual. Catalytic hydrodesulfurization is the commonly used process, but it remains unsatisfactory from economical and technical point of view. When desulfurization of oil and coal is considered, the ion-radical methods take on attraction. There are works on using the naphthalene anion-radical salt with the potassium cation (Chatterjee et al. 1991) or transition metal as reducers (Startsev 1995). Aliphatic sulfur-containing compounds pass into anion-radicals, which undergo carbon–sulfur splitting with the formation of water-soluble metal mercaptides (Borah 2004, 2005). However, anion-radicals of aromatic thiaheterocycles do not lose sulfur and remain in fuel. The aliphatic-to-aromatic difference is also operative for cation-radicals: Aliphatic ones eliminate sulfur and form carbocations, which react with solvents giving rise to soluble compounds (Park and Lee 2003). In aromatic cation-radicals, a positive charge is preferentially localized in the aryl rings but not on the sulfur atoms (see, e.g., Dyusengaliev et al. 2005). This prevents elimination of sulfur.

According to Eish et al. (1986), the complex resulting from the interaction of (2,2′-bipyridyl)(1,5-cyclooctadiene)nickel with lithium aluminum hydride in THF, is a powerful desulfurization agent for such aromatic sulfur heterocycles as dibenzothiophene, phenoxathiin, phenothiazine, and thianthrene. The reaction leads to ring opening or ring contraction desulfurized products in high yields. The ring-opening products are biphenyl, diphenyl ether, diphenylamine, and benzene, whereas the ring-contraction products are dibenzofuran and carbazole. The desulfurization proceeds through single-electron transfer mechanisms and anion-radicals of the sulfur-containing heterocycles were proven as crucial reactive intermediates. A decisive peculiarity of such a reductive system consists in combination of electron transfer with coordination of the resulting anion-radicals to the metal center having especial affinity to sulfur. In this sense, recent work by Huang et al. (2004) on cuprous chloride-based ionic liquid should be mentioned. The liquid was synthesized by mixing 1-butyl-3-methylimidazolium chloride with copper monochloride. As established, copper(I)

anionic species are formed, such as $CuCl_2^{2-}$, $Cu_2Cl_3^-$, and $Cu_3Cl_4^-$. Imidazolium salts with these anions are moisture insensitive, stable in air, and as ionic liquid, possess powerful extractabilty. The liquid effectively removes thiophene and its derivatives from motor fuel at the expense of one-electron reduction, complexation, and extraction of these deleterious admixtures.

Bernal and Caero (2005) intentionally used the static effect of polar organic solvents for oxidative-extractive desulfurization of thiophenic components from diesel fuels. Namely, the mixture of diesel fuel and an organic solvent was treated with hydrogen peroxide and vanadium catalyst. As established, oxidation occurs only after extraction of the sulfur compounds from the fuel into the organic solvent. The more polar is the solvent, the deeper desulfurization takes place. For instance, the desulfurization reaches 85% in DMF and only 30% in acetonitrile. The authors underline that the solvent participates in reaction by creating a medium that facilitates electron transfer between the reactive species involved, which improves the oxidation activity. The claimed method allows separating benzothiophene, dibenzothiophene, 4-methyldibenzothipohene, and 4,6-dimethyldibenzothiophene. These components are classified as refractory ones because they are not removed within the state of the art desulfurization technology by catalytic reactions with hydrogen. It needs to underline that the industrially developed countries plan to reduce gradually the statutory sulfur content in diesel fuel. In the United States, for example, this content is limited with 350 ppm to reach 10 ppm in the contemporary time (EPA420-R-00-026, December 2000, U.S. Environmental Protection Agency). Even for the 350 ppm specification, the diesel fuel range available today has low total sulfur content but an out-of-proportion high concentration of refractory sulfur species such as the benzo-fused thiophenes mentioned in this section. The claims adduced here give solutions of the problem.

8.8 CONCLUSION

Although ion-radical organic chemistry is a new branch, its development reaches an "outlet" stage in the sense of practical applications. Some of them have already brought commercial advantages; others remain as promising fields with attractive prospects. Further development of ion-radical organic chemistry will surely proceed along with the search of new applications.

In general, why do scientists call their job research when they are looking for something new? Because they want to proceed on the basis of their previous achievements. In addition, every researcher wants to realize a practical application for results already obtained. However, this author knew one mathematician who had created an elegant and quite general theory, of which he was justifiably proud. When asked about possible applications of the theory, he answered, "How can you talk about that? My theory is so general that any particular use is impossible." Pure mathematics probably tolerates such an approach—maybe it is even acceptable. However, chemistry is different; both scientific interest and practical necessity are the driving forces for development.

The example of an anion-radical concept of lubrication is symptomatic. Current interest in biological electron transfer will undoubtedly result in new ways to design drugs. Data on reversible isomerization of ion-radical species will lead to a widening of material choice for "electron memory" systems. Many other field of applications are also possible. Knowledge of the laws of ion-radical chemistry opens a way to optimize many organic reactions, as it was shown in Chapter 5. Currently, such a chemical process is applicable in industry that is justified by economics, including product yields, time of their manufacturing, costs of reagents and energy bearers. All the points are subjects of contribution from ion-radical chemistry. Wood delignifaction and fossil-fuel desulfurization are prominent examples.

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9 General Outlook

9.1 IMPORTANCE OF ION-RADICAL ORGANIC CHEMISTRY

This is the time to emphasize some general and important topics of ion-radical organic chemistry and formulate some problems that are present today and await solutions. Those topics that could open up new chemical routes (but whose generality and, sometimes, applicability are presently unclear) should also be scrutinized.

Single-electron transfers to or from organic molecules result in the formation of anion- and cation-radicals, respectively. The removal of an electron from the bonding highest occupied molecular orbital (HOMO) or electron transfer to an antibonding lowest unoccupied molecular orbital (LUMO), respectively, leads to weakening of the corresponding bond. The bond becomes easier to break. The unpaired spin and charge can delocalize within the molecular carcass and this results in its flattening. An unpaired electron can be localized on a functional group (atom), which leads to a change in the substituent effect. Appearance of an unpaired electron is accompanied with the emergence of an electric charge. The spin and charge can be delocalized together among the molecular constituents or spatially separated as in the distonic species. Each type has its own synthetic opportunities, which are discussed in the earlier chapters. This book as a whole shows that ion-radicals cannot be treated either as conventional radical particles or ionic species. They are characterized by a unique behavior. This is why this book uses the hyphen-bound term *ion-radicals* in contrast to the term *radical ions*, which is accepted in the Chemical Abstracts Classification Code.

9.2 SCIENTOMETRIC NOTES

Throughout this book, numerous examples have been presented. However, the purpose was not to write a comprehensive review or recount the historical development of ion-radical organic chemistry. The examples, selected from a large number, were chosen to describe the phenomena and not the species. Such an approach made it impossible to refer all the papers dealing with organic chemistry of ion-radicals, or even to cite all the good papers. At several places of the book, conflicting literature data and inconsistent theories are described along with alternative interpretations of published findings. In some cases, more experimental and theoretical works have been recommended. Because the coverage was selective by necessity, recent examples have been highlighted in most part of the book. Thus, this issue is thoroughly updated.

A numeric analysis of references from subject indices of Chemical Abstracts leads to the following estimations: The average time of publication doubles every 4 years, rather than the normal period of 10 years. The number of references to works from the ion-radical field, appearing in papers on general organic chemistry, doubles on an average every 2 years. As for individual authors, the most productive ones are, as a rule, also the most cited. The information noise generated here is considerably lower than in other fields. The frequency of the transfer of concepts and terms from the ion-radical organic chemistry to the general organic chemistry is quadrupled every 10 years. More and more new groups are getting involved in this field, and many of these groups bring their own ideas or discuss earlier results from new viewpoints. Ion-radical organic chemistry is in a phase of rapid development and a high level of attention can be predicted for a foreseeable future.

It is obvious that ion-radical organic chemistry attracts much attention. It has developed intensively. Achievements in this field echo and are rapidly absorbed into the general stream of organic chemistry.

Colleagues often inspire one another in their professional undertakings. On comparing the materials collected after 2001, it is clear that the process of intellectual bridge building develops with time.

Some notes on the papers quoted need to be addressed. The papers cited generally contain a majority of the conceptual references. A reference is qualified as conceptual if the cited work is used as a source of idea of a given research. This is a direct manifestation of ethical duty with respect to colleagues. Operational references are also relevant. These references are necessary to obtain new scientific results. Evolutionary references are frequently included; they combine preceding works in mini reviews. Such references reflect the background of a specific problem that a paper is devoted to. It is a fact that a majority of the evolutionary citations are copied from one paper to another, often with the same errors or inaccuracies. It is true that such a phenomenon is common for publications in all the sciences. Simkin and Roychowdhury (2007) even derived a special mathematical description of such a branched process. The Matthew effect also works in the field considered. Papers issued by influential scientists are cited more often than the publications of ordinary researchers although the latter presented results of more relative significance. (The term *Matthew effect*, from the gospel, is ascribed to the evangelist Matthew whose maxim sounds in common language as "It becomes better for them who is already doing really well.")

In any event, the scope of citation within the framework of the publications analyzed favors the formation of a specific association—the so-called invisible college of ion-radical organic chemistry. Not only formation but also widening of this invisible college is crucial for solving the problem. This is why the people of the invisible college, working in the field of organic ion-radicals, should not be a tightly meshed community that selects its own society and then shuts the door. Zuccala (2006) gives a very fair definition of invisible colleges.

> An invisible college is a set of interacting scholars or scientists who share similar research interests concerning a subject specialty, who often produce publications relevant to this subject and who communicate both formally and informally with one another to work towards important goals in the subject, even though they may belong to geographically distant research affiliates.

All the contributors could not be exhaustively cited within the volume that is resonable for this book. Exhaustive citation would be a colossal task. More importantly, dazzling information will not be useful for readers. Nevertheless, the book supposedly shows that the invisible college definitely exists in ion-radical organic chemistry and will continue to exist in our increasingly global society. One of the aims of this book is to make such an invisible college more visible and give the hope that it can really solve the remaining and arising problems.

9.3 PROSPECTS

This book concentrates on organic ion-radicals and their reactivity. However, readers should be cautioned against considering all organic reactions as inevitably including ion-radical mechanisms. (Note the following proverb: When the only tool you have is a hammer, every problem begins to look like a nail.) Attempts to cover all the organic reactions with the ion-radical *blanket* have already been undertaken (Bielevich and Okhlobystin 1968). Organic chemistry, living and developing, requires no preconceived theories or approaches.

Scientific research has led to significant success in practical applications of organic ion radicals. Throughout the book, it was demonstrated the possibilities of ion-radical organic chemistry in solving preparative, large-scale manufacturing, and fossil-refining problems. Such applications should be explored further in future. It is very important to concentrate efforts on the elaboration of synthetic methods of ion-radical organic chemistry. The correct choice of new developmental procedures opens up a wealth of new directions. It is hoped that interest in this area will continue to bring new ideas and reactions, particularly in the area of organic synthesis in liquid phase and without light irradiation.

Owing to the contemporary development of density functional methodology and ever-increasing computing power, the interplay between experiment and theory promises significant progress. This will bring new insight into technical problems connected with smart nanoelectromechanical systems. These molecular-sized systems exhibit properties that are interpretable in terms of classical mechanics. Being reduced/oxidized, the components can move one relatively another. The main characteristic of these systems is their reversibility and bis-stability in terms of the initial and final positions of moving moieties. In these systems, ion-radicals are formed and undergo further reversible reduction or oxidation. Such deep redox reactions control relative motion of organic constituents (depolarizers) along a predefined path. Chemistry of multielectron transfers is beyond of the scope of this book (The molecular motors based multi-electron transfer chemistry are considered in works by Sauvage 2001 and Balzani et al. 2003; see also Asfari and Vicens 2000, Ward 2000, Tolksdorf et al. 2002, Carella et al. 2003, van Delden et al. 2003, Mandl and Koenig 2004, and Balzani et al. 2004).

It would be expedient to widen synthetic applications of distonic ion-radicals. In principle, they allow developing dual reactivity—at the sites of radical unsaturation and, separately, of charge localization. The sterical aspects of ion-radical organic chemistry can also be estimated as intriguing, but they are insufficiently developed. The so-called confined ion-radical organic chemistry promises serious perspectives, too.

It is not surprising that there are a lot of unsolved problems faced by the considered field. Advances in science cannot, principally, be completed once and for all. Solution of one problem leads to others. In the world of science, patience means more and yields more than just inspiration.

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